Different aspects regarding the surveillance of surgical site infections

DIFFERENT ASPECTS REGARDING THE **SURVEILLANCE** OF **SURGICAL SITE INFECTIONS**

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Colofon

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“Do what you can, with what you have, where you are”

Theodore Roosevelt

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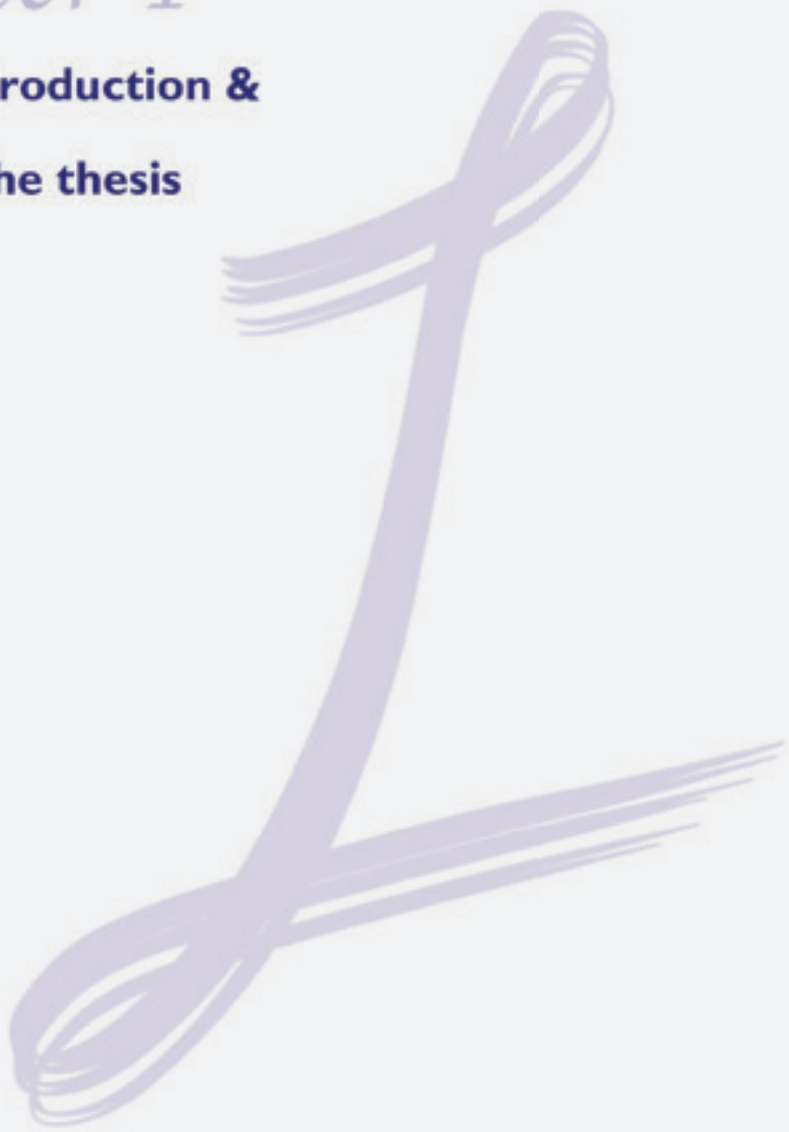
Chapter 1

General introduction & outline of the thesis



Surgical site infections – general

Health care-associated infections (HAIs), also referred to as nosocomial infections, are *"infections that patients acquire during the course of receiving health care treatment for other conditions"* [1]. The infectious signs and symptoms are neither present nor incubating upon the patient's admission to the hospital, but become manifest after forty-eight hours (after admission), or after the third calendar day of admission to the health care facility [2, 3]. HAIs received lots of public attention during the last decade, as the consequences of these infections have a significant impact on health-related quality of life. HAIs result in delayed wound healing and increased use of antibiotics, hospitalisation days, and health care costs. Furthermore, HAIs are a significant burden in terms of patient morbidity and even mortality [2, 4-10].

Surgical site infections (SSIs) are the most common hospital-acquired infections in surgical patients and account for approximately 17% of all HAIs. Other common nosocomial infections are urinary tract infection, infections of the bloodstream, pneumonia, skin, gastrointestinal tract, and central nervous system [3, 11-13] (Figure 1).

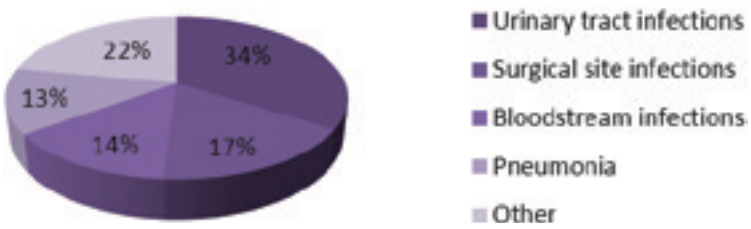


Figure 1: Types of health care-associated infections in hospitals
Source: Center for Disease Control and prevention [14]

Surgical site infections, also called surgical wound infections, are defined by the Centers for Disease Control and prevention (CDC) [8] as *"infections occurring within thirty days after a surgical operation (or within one year if an implant is left in place after the procedure)"* [1].

As the infection of the surgical site may occur at any depth, the CDC classified the infections into superficial, deep and organ/space infections. A superficial SSI

involves only the skin or subcutaneous tissue of the incision. If the deep soft tissues of the incision are involved, then the infection is considered a deep SSI. An organ/space SSI involves any part of the body, other than the incision, opened or manipulated during the operative procedure [1] (Figure 2).

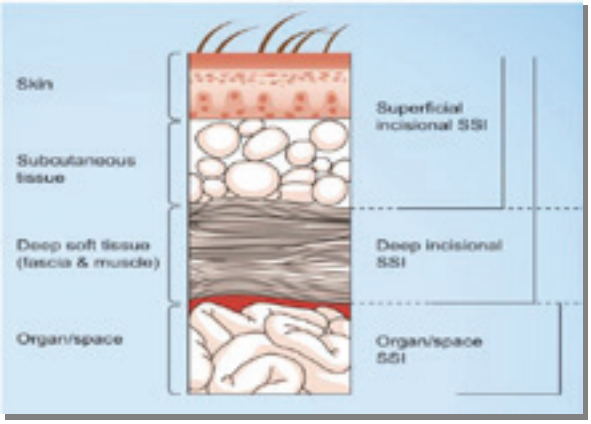


Figure 2: Types of surgical site infections
Source: Center for Disease Control and prevention [14]

Superficial SSIs are the most common SSIs and are generally treated locally. Treatment of deep or organ/space infections often requires more invasive treatment, such as intravenous antibiotics, drainage procedures or re-operations [9].
According to a national study with currently over 90 participating hospital in the Netherlands, the prevalence of SSI was 5.5% among all hospitalised surgical patients [15]. This percentage is comparable to studies in other European countries with SSI rates ranging from 3.5 to 11.6% [5, 16-21].

Risk factors surgical site infections

Despite many efforts to prevent the risk of HAIs, SSIs remain a serious problem in health care settings. Over the past decades, many studies have been performed worldwide to identify the multifactorial risk factors of SSIs [22, 23]. Some factors are non-modifiable, others are modifiable, and some are patient-related, while others are surgery- or environment-related [24, 25]. Knowledge of the individual risks of SSIs is important for two reasons: 1) to decide which targeted prevention

and surveillance methods should be implemented, and 2) it contributes to better interpret the comparisons of SSI outcomes between different health care facilities, surgical disciplines or patient populations.

Patient- and surgery- or environment-related non-modifiable risk factors of SSIs

Examples of non-modifiable patient-related risk factors are obesity, comorbidities (e.g., diabetes mellitus and inflammatory bowel disease), smoking behaviour, existing infections at surgical site, the patient's immune response, the ASA-score (American Society of Anaesthesiologists), age and gender of the patient [24-26].

Obesity, defined by the World Health Organization (WHO) as having a body mass index of more than 30 kg/m^2, has been identified as a major risk factor of SSIs, with the highest rates in morbid obese patients [27-29]. The higher the Body Mass Index (BMI), the higher the chance on an SSI, as obese patients are inefficient in energy expenditure, have an impaired immune response, and a decreased circulation into fat tissue [30, 31].

With regard to age, the outcome of an SSI among elderly patients is worse than in younger patients, due to the diminished host response and the increasing risk for post-operative morbidity and mortality [32]. Additionally, ageing comes along with a decline in muscle mass, muscle strength, and muscle quality, a condition termed by Rosenberg in 1989 as sarcopenia [33]. Involuntary weight loss is common in the elderly and results in poor outcome, revision surgery, use of non-steroidal anti-inflammatory drugs, and may extend the duration of surgery [8, 34]. As to gender, several studies described a higher risk of SSI in male patients compared to women. An explanation could be the biological differences between men and women regarding skin and/or other anatomy [43, 44]. Co-morbidities are found to be associated with SSIs, with diabetes mellitus as the most frequently considered one [35]. Another population at risk are patients undergoing surgery for inflammatory bowel disease (IBD), i.e., Crohn's disease or ulcerative colitis, due to immunosuppressive therapy [36-38].

Smoking has been associated with delayed wound healing and weight loss, compromised immune and respiratory system, and an increased risk of mortality [39-41].

Finally, the ASA-score is a classification system to evaluate the patient's medical status prior to a surgical procedure, based on class 1 to 6: class 1) a healthy patient, class 2) a patient with a mild systemic disease, class 3) a patient with a severe systemic disease, class 4) a patient with a life-threatening disease, class 5) a patient

with a life expectation less than twenty-four hours with or without surgery, and finally class 6) a patient who is brain-dead [42]. An ASA-score of 3 or higher is associated with a high risk of developing SSIs [37, 43].

Surgery-related factors that are not modifiable include the complexity of the surgical procedure, previous surgery, size and type of the health care facility, type of surgery (e.g., elective or acute) and surgical wound class (clean, clean-contaminated contaminated or dirty) [44, 45].

The complexity of the surgical procedure determines the position and size of the surgical site. Laparoscopic surgery is an example of surgery using very small incisions, whereas more complex surgery, such as colorectal surgery, may require a larger incision. It has been shown that colorectal surgery is associated with a high risk of SSI due to the probability of bacterial contamination from the colon, with rates of SSI as high as 26% [46-50]. After vascular surgery SSI rates vary between 4% and 25% [51, 52]. This variation may be explained by factors, such as their underlying vascular disease and multiple co-morbidities. Also peri-operative events contribute to the increased risk after vascular surgery, such as the implantation of a vascular graft or other foreign material. This foreign material creates a micro-environment that is convenient for bacterial attachment and colonization and thereby protects causative potential pathogens from the host defence and from antimicrobial therapy (Figure 3).

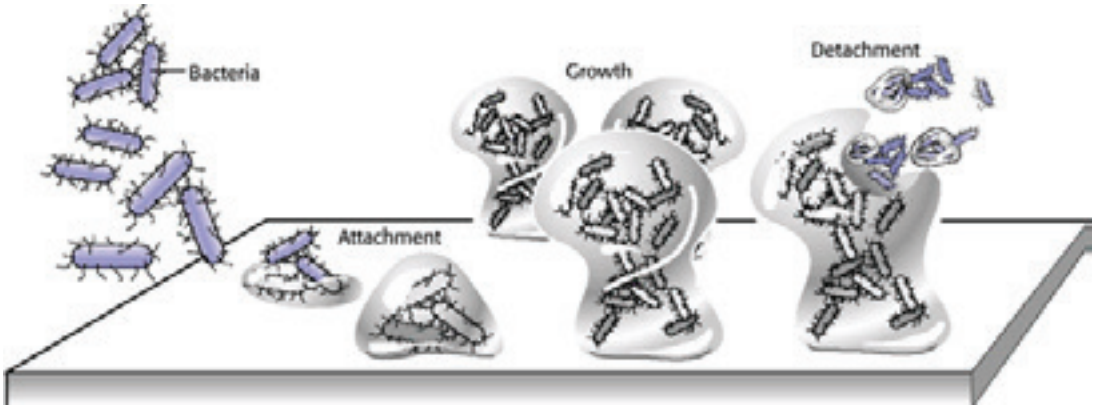


Figure 3: Illustration of the biofilm bacterial colonization process.
1) The bacteria need to find an inert surface (e.g., implant). Implants or dead tissue that have been integrated by the host with some type of surface are not inert and will resist colonization. 2) The colonization process will continue until mature colonies are formed. 3) Once mature, the colonies can change based on environmental signals or signals between colonies.
Source: Rockwood & Green's Fractures in Adults, 6th Edition. Chapter 18: *Local Complications*, Kirti D. Moholkar & Bruce H. Ziran. © 2006 Lippincott Williams & Wilkins.

Other surgery-related risk factors are failed arterial reconstruction and presence of a groin incision [51, 53-55].

With regard to the size and type of the hospital, higher infection rates are described in large and university hospitals, very likely due to an unfavourable case-mix of patients and the limited experience of the surgeons in training [56]. The CDC classified type of wound into four wound classes, i.e., clean, clean-contaminated, contaminated and dirty, according to the likelihood and degree of bacterial contamination of the wound at the time of the surgical procedure, and other wound characteristics, such as size, depth, and location [1, 57] (Table I). Emergency surgery and dirty/contaminated surgical wounds yield higher SSI rates than elective surgery or clean surgical wounds [45, 58, 59].

Table I: Definitions wound classifications by the Centers for Disease Control and prevention

Wound class	Contamination of the surgical wound
1. Clean:	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow non-penetrating (blunt) trauma should be included in this category if they meet the criteria.
2. Clean-Contaminated	An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
3. Contaminated:	Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered are included in this category.
4. Dirty	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing post-operative infection were present in the operative field before the operation.

Source: Centers for Disease Control and prevention [14]

There is a clear relationship between infection rates and wound class from clean to dirty. Clean wounds, e.g., after vascular surgery, have a 1-6% rate of SSI. Clean-

contaminated wounds, e.g., after a gynaecologic procedure, have a 3-11% rate. For, contaminated wounds, such as wounds after laparotomy with intestinal spillage, 10-17% rates of SSI have been determined. And finally dirty wounds, after abdominal exploration for intra-abdominal abscesses, show infection rates of more than 27% [60-62].

Culver *et al.* [52] created a risk classification system, known as the NNIS (National Nosocomial Infections Surveillance) risk index. The system combines the CDC's wound classification, of either contaminated or dirty, with procedure-specific excessive operative time and an ASA-score of 3 or higher. Additionally, the system is widely used, operation-specific and a good method to correct for differences in patient case-mix [52, 63]. After introduction of antibiotics prophylaxis in the 1950s [64], the SSI rates decreased to 2.1% in clean wounds, 3.3% in clean-contaminated, 6.4% in contaminated, and 7.1% in dirty wounds [52]. There is, however, considerable variation in SSI within each class according to the type of surgery being performed [59] and some authors acknowledge deficiencies of the NNIS index with regard to the lack of other important risk factors of specific procedures that primarily need to be identified and incorporated [65].

Patient- and surgery- or environment-related modifiable risk factors of SSI

Most healthy people, approximately 30%, are carriers of the bacterium *Staphylococcus aureus* in the nose. Nasal carriage of *S. aureus* is a major risk of SSIs, especially for those patients who received an implantation following vascular of orthopaedic surgery [66-68].

Patients can be treated pre-operatively to diminish the chance for developing an SSI caused by *S. aureus*. Eradication of *S. aureus* prior to surgery can be achieved with nasal mupirocin ointment and chlorhexidine showers and has shown to decrease the occurrence of SSIs, significantly for cardiothoracic patients [68-73].

Other modifiable patient-related risk factors that are commonly present among older patients include nutritional status [24, 74, 75]. Patients who are malnourished are at a high risk of surgical complications. Malnutrition is associated with causes of SSI, such as, impaired host immune response and low serum albumin level, and result in higher morbidity, delayed recovery and longer hospitalisation, mortality, and higher health care costs [76, 77]. Peri-operative nutritional supplements, such as provision of calories, proteins, electrolytes, vitamins and minerals, have been described to adjust the immune and inflammatory response of the malnourished patient [78, 79].

Other pre- and peri-operative measures include antimicrobial prophylaxis, disinfection of the patient's skin, not shaving of the surgical site and normothermia during surgery. Surgical antimicrobial prophylaxis refers to the small administration of an antimicrobial agent, given 15-60 minutes before the surgical incision. Timing, choice and duration of prophylaxis should be based on guidelines [80]. With regard to the skin preparation, duration of the surgical scrub and the type of skin disinfectant influence the development on SSIs. Several antiseptic agents are used for pre-operative skin preparation at the incision site and include products containing iodine, alcohol or chlorhexidine gluconate, all with broad-spectrum antimicrobial activity [81, 82]. Pre-operative hair shaving of the surgical site has also been associated with a significantly higher SSI risk of SSI than either the use of depilatory cream or no hair removal at all [14, 82]. Hypothermia is a fall in body temperature below 36 degrees and is one of the most common risk factors of SSIs. The best way to avoid hypothermia is to achieve normothermia during surgery by active warming, in order to maintain the core temperature of the patient and to prevent vasoconstriction and decreased blood flow to surgical sites [83].

Thus, by far the most important surgery- or environment-related modifiable risk factor of SSI is the (lack of) adherence to the above and other measures. Due to the difficulty to change behaviour of the health care staff, adherence to guidelines and protocols is frequently suboptimal [84, 85], for example, incorrect use of nose- and mouth masks, the incorrect use of surgical clothing and drapes, and wearing jewellery [9, 86, 87]. Moreover, hand hygiene by health care staff, one of the most effective means to prevent SSIs, has a poor compliance [88, 89]. Reasons not to adhere to infection preventive guidelines include insufficient time, inaccessibility to hand hygiene supplies, irritating agents, lack of knowledge of guidelines, negligence, and understaffing [90, 91]. Continuous instructions and training on the guidelines and feedback on the results of the measurements are needed to improve compliance [92].

Other surgery- or environment-related modifiable risk factors are a prolonged pre- and post-operative stay. Patients who are less physically capable and have a greater in-hospital exposure time are at an increased risk for developing SSIs. An explanation is the widespread use of antibiotics that can lead to antibiotic-resistant microorganisms being present. Also, many patients are treated in the same hospital area that might provide an opportunity for microorganisms to spread between them and cause infections [25, 93].

Duration of the surgical procedure can be influenced by factors, such as the experience or skills of the surgeon in charge and the complexity of the procedure [94]. The length of the operation has also been identified as a risk factor of SSIs. Procedures longer than 3-4 hours showed to increase the risk of SSIs substantially, as longer operation duration allow for more personnel traffic and thereby negatively affecting the air flow in the operating theatre [25, 95].

Microbial spectrum of surgical site infections

During a surgical procedure the patient's skin barrier is breached and bacteria from the skin and the direct environment are able to enter the wound, colonize the wound, and eventually cause an infection [51]. Besides the positive association between antibiotics, the patient's immune system and causative pathogens, antibiotics can also directly negatively interact with the immune system and increase the risk for an infection [96, 97].

Which microorganisms are involved in SSIs depend amongst others on factors, such as the wound type, the depth and location, the degree of tissue perfusion, the host immune response, but also the adherence to guidelines with regard to the choice of antibiotic prophylaxis and hygiene measures [98, 99]. The hands of health care staff may become constantly colonized with pathogenic flora, e.g., *S. aureus* and gram-negative bacilli [100].

As previously mentioned, *S. aureus* from the patient's skin flora is the most frequent cause of infections associated with clean surgical procedures, e.g., vascular procedures [51, 101]. Other common bacteria in clean surgeries are coagulase-negative staphylococci, *Escherichia coli*, *Pseudomonas aeruginosa*, enterococci, *Proteus* species, *Klebsiella pneumonia* and streptococci [53]. In contaminated and dirty procedures, e.g., colorectal procedures, the microorganisms are even more diverse and the predominant organisms include gram-negative rods and enterococci besides skin flora [80, 102].

Surgical antimicrobial prophylaxis is recommended prior to the incision in many cases. The higher diversity of potential pathogens in contaminated wounds compared to clean wounds is an argument for broad-spectrum of antibiotic coverage [14]. The choice of antibiotics depends on the antimicrobial agent's pharmacokinetics and pharmacodynamics, the patient's medication allergies, and the required spectrum of antimicrobial activity [103].

According to evidence-based guidelines antimicrobial prophylaxis must meet the following requirements: 1) an appropriate choice, that is be based on the

susceptibility of the expected microorganisms, 2) a correct dosage, 3) administration at the right time (15-60 minutes prior to incision), and 4) no antibiotic administration after 24 hours post-operatively to diminish adverse effects and antibiotic resistance as much as possible [14, 103]. In the Netherlands, the Dutch Working Party on Antibiotic Policy SWAB (Dutch acronym: *Stichting Werkgroep AntibioticaBeleid*) has developed guidelines for the therapeutic and prophylactic use of antibiotics for hospitalised patients, aiming at the optimal use of antibiotics and the control of antibiotic resistance.

The increase of resistant microorganisms is a global concern. Factors that contribute to this phenomenon are the unrestricted availability of antibiotics in many countries, inadequate stewardship of antibiotic prescription [104]. As a result of resistance, antimicrobial treatment and hospital stay are prolonged, and therapy costs are increased [9, 102]. In the Netherlands, where the rate of antibiotic consumption in humans is low, resistance due to Extended-Spectrum Beta-Lactamases (ESBL's) in enterobacteriaceae, is emerging [105]. Thus, surveillance data on the causative microorganisms of an SSI and the antimicrobial susceptibility patterns are important to understand the scope and magnitude of the emerging antimicrobial resistance and to make an optimal choice.

Prevention of surgical site infections

Strategies for the prevention of SSIs are based on reducing the risk of bacterial contamination and consequently the development of SSI [9]. Many of the patient- and surgery-related risk factors are mentioned above, but only some factors are modifiable [87].

In the past 10 years, several organizations have developed programs with the aim to decrease rates of post-operative complications, including SSIs. Special attention has been paid to a so-called bundle approach, an approach combining several patient- and procedure-related risk factors, to reduce the chance on an SSI after the surgical procedure [9, 89, 106]. Pre-operative strategies are intended to optimally prepare the patient before incision, such as the use of appropriate antisepsis and hand hygiene before incision for all surgical team members. Other preventive strategies are focussed on environmental and factors, such as ventilation of the operating theatre, and cleaning and disinfection of environmental surfaces. Examples of post-operative care are protection of an incision site with

sterile dressing and washing hands before and after any contact with the surgical site [9, 101].

In the Netherlands, hospitals currently participate in a national programme intended to improve patient safety, i.e., the patient safety programme VMS (Dutch acronym: *VeiligheidsManagementSysteem*). The programme consists of eleven targets, one of which is the prevention of SSIs. To achieve this, a bundle of four evidence-based interventions is to be implemented, assuring compliance by means of repeated measurements of the behaviour of the health care staff. The goal is to achieve a compliance of at least 90% [85, 107, 108]. The elements of the bundle are (1) no pre-operative hair removal of the patient, (2) correct timing of pre-operative administration of prophylactic antibiotics, (3) peri-operative normothermia, and (4) restricted entry and door movements during the surgical procedure. The choice for these elements was based on guidelines issued by the Dutch Working Party on Infection Prevention WIP (Dutch acronym: *Werkgroep InfectiePreventie*) and were systematically reviewed in the literature regarding the evidence for their efficacy [109, 110]. First, pre-operative hair removal includes shaving, clipping or creams. As shaving before incision is associated with a higher prevalence of SSI compared to clipping [111], CDC and WIP recommend removing body hair only in case of surgical technical reasons. In case hair has to be removed, CDC and WIP recommend the use of a clipper [14, 110, 112]. Antibiotic prophylactic antibiotics have been shown to prevent the development of SSI, although several factors (as the appropriateness, timing, dosage, duration and route of prophylaxis administration) can hamper its effect [113]. As mentioned before, the optimal time for administration preoperatively is between sixty and fifteen minutes before surgical incision. The choice of the antibiotic dosage and duration depend on the type of surgical procedure and the expected microorganisms [80, 103]. Third, achieving normothermia by active warming has been shown to decrease surgical site infections after surgery [114, 115]. Finally, the WIP advises to limit the number of personnel present in the operating theatre and to limit the traffic in and out the operating theatre during the surgical procedure [110]. It has been shown that compliance with a bundle of infection preventive measures significantly decreases the SSI rate [85] (Figure 4).

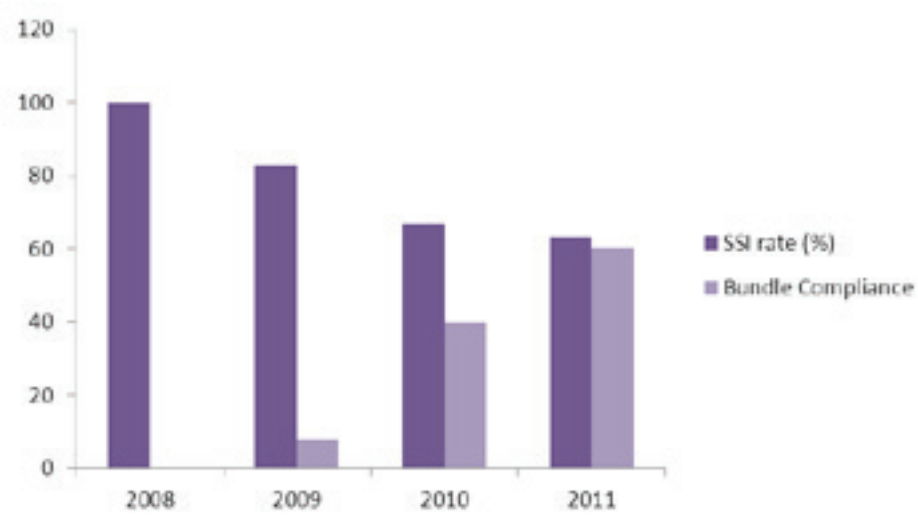


Figure 4: Annual changes in the surgical site infection (SSI) rate and bundle compliance and the 95% confidence interval.
Footnote: 2008 was taken as the reference year of SSI and the relative changes after adjustment for confounding variables are provided [85]

Infection Surveillance and Control

A surveillance program is essential for the detection of SSIs and determination of the SSI rates in health care institutions. Surveillance of SSI and giving feedback of relevant data to surgeons has been shown to reduce SSIs [14, 116, 117]. As it is expected that variation in SSI rates depends on the type of hospital and patient case-mix, it is important that infection criteria are clearly defined and that methods for data collection are standardised [118-121].

In 1974 the CDC initiated a nationwide study to infection control procedures, known as the SENIC (Study on the efficacy of nosocomial infection control) Project. The primary objectives were (1) to determine whether the implementation of infection surveillance and control programmes decreased the number of nosocomial infections, (2) to describe the present status of those programmes and the infection rates, and (3) to determine the relation between characteristics of hospitals and patients, elements of the infection control programmes, and variations in the infection rate. The project showed that with accurate infection control activities and routine feedback to the medical staff, infection rates significantly decreased by 30% [122].

In general, surveillance during hospitalisation, also called in-hospital surveillance, is performed for each patient who undergoes surgery. Infection control personnel routinely collects data from the patient's medical records and consultations with the surgeon in charge, i.e., demographic patient characteristics, data on the surgical procedure, risk factors of SSI, bacteriological data by cultural assessment, and any signs for an SSI based on national and international criteria regarding the assessment of SSIs [1, 123]. However, as the trend towards shorter length of stay is increasing, a higher proportion of SSIs manifests after discharge [124]. As a result, postdischarge surveillance (PDS) has become increasingly important. The performance of in-hospital surveillance alone will result in an underestimation of the actual one [119, 125-127].

For each individual patient, a surveillance period of thirty days after surgery is recommended to ensure accurate information concerning the development of SSI, in patients without an implant. The choice of thirty days was based on prevalence studies showing that between 12% and 84% of all SSIs are detected after discharge of the patient from the hospital [12, 121, 125, 128]. In case an implant is in place the follow-up period is extended to one year, because implant-associated infection can manifest much later [14, 25, 129].

In the Netherlands, a national nosocomial surveillance programme was developed in 1996, known as PREZIES (Dutch acronym: *Preventie van Ziekenhuisinfecties door Surveillance*). The PREZIES programme consists of a standardized surveillance system in participating hospitals, during and after hospitalisation, collects reference data for national policy-making, and creates a base to stimulate further intervention research [15, 130]. As a result, benchmarking data is offered to the participating hospitals.

Postdischarge surveillance can be performed actively or passively. The active method includes direct observation of the surgical site by health care staff, e.g., an independent infection control nurse who is familiar with the definition of an SSI, to discuss wound signs and symptoms. This is carried out during morning shifts and in different sections of the medical and surgical wards. Direct observation has seemed to be a reliable surveillance method, but can be time-consuming and is often only feasible if the follow-up after surgery occurs at the health care facility where the procedure was performed [131]. Other examples of active surveillance are telephone interviews with patients and questionnaires about the patient's surgical wound by infection control nurses. Disadvantages of questionnaires is that not all are returned, and that surgeons and infection control nurses are not always in

agreement regarding the diagnosis of SSI [132]. Additionally, self-assessment of the surgical wounds, either by a telephone interview or questionnaire, may not always be reliable due to information bias [127, 131, 133, 134]. Although patients are able to report signs and symptoms of the wound, the assessment does not always reflect the clinical interpretation of the infection control nurse [134].

The passive surveillance method is used when the health care worker checks the patient's readmissions of SSI or contacts medical staff for medical or nursing reports of infection, e.g., detection of an SSI when patients are (re-) hospitalised or examination of the outpatient medical record [125, 126]. This method is often used in hospitals, as it is achievable and reliable. Although this passive method requires different physical and human resources, the return rate of the data seems to be acceptable, because almost every patient is seen by their surgeon during hospitalisation and after discharge [127].

Depending on the surveillance method used and the type of surgery, different rates of SSI are found after discharge ranging from 12 to 84% [127]. A study to SSIs after vascular surgery with a passive surveillance method showed that almost 50% of all SSIs was found after discharge within thirty days [135], up to more than 50% within ninety days [136], while others found lower amounts of 25% or less. With active surveillance up to 43% of all SSIs can be found within thirty days after discharge [125, 137]. The figure below shows a peak incidence of SSI during the first (mainly during hospitalisation) and second (mainly postdischarge) postoperative week. The study found that 90% of the superficial SSIs was detected at day 25, and 90% of the deep SSIs was detected at day 122 (Figure 5).

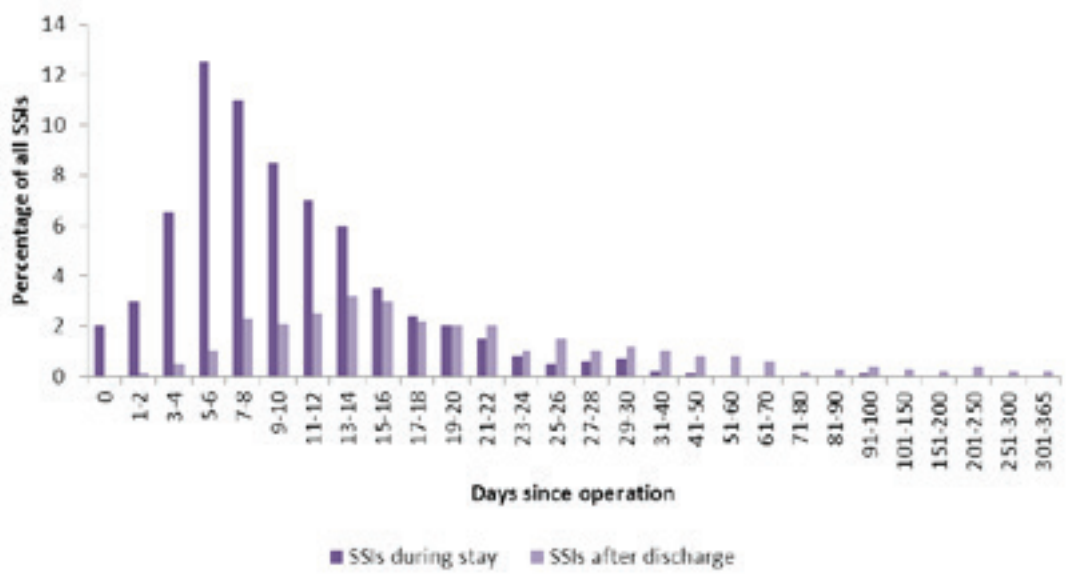


Figure 5: Time curve showing the percentage of all SSIs (both superficial and deep, with data from all procedures and all Postdischarge Surveillance methods together) that developed during hospitalisation and after discharge, by post-operative day.
Source: Manniën *et al.* (2006) [125]

Aims and outlines of this thesis

This thesis was written with the aim to diminish the risk of patients within a health care facility for developing surgical site infections. Throughout the thesis, data to assist health care personnel in reducing infections associated with health care is provided, by describing the assessment, planning, implementation and evaluation of a Dutch safety management system, the VMS safety bundle. Surveillance methods for SSI and the assessment of compliance with infection control measures are crucial, including standardised definitions of SSI, consistent classification criteria, the ability to detect SSIs after discharge, the ability to adjust for differences in the severity of illness between patient populations, and the assessment of microbiological laboratory data to identify bacteria and patterns of susceptibility to antibiotics.

In **chapter 2**, we retrospectively assessed the incidence of SSI after gastrointestinal surgery during and after hospitalisation, and evaluated the (in-) efficacy of the VMS safety programme, designed at an academic medical centre, on the incidence of SSI. To achieve this, an analysis based on a logistic regression model to determine risk factors for SSIs after gastrointestinal surgery was performed. In **chapter 3**, we retrospectively analysed the microbiological results of the wounds after gastrointestinal surgery, i.e., the microorganisms isolated from wound swabs and blood samples, as well as the antimicrobial susceptibility, and discussed the appropriateness of the prophylactic antibiotic choice. In **chapter 4**, a cohort study was conducted to determine the incidence and risk factors for SSIs after vascular surgery and the effect of the Dutch VMS safety bundle on the incidence of SSI was evaluated. In addition, the most frequently isolated microorganisms involved were determined, as well as the antimicrobial susceptibility patterns of the bacteria associated with SSIs. Finally, in **chapter 5**, we retrospectively investigated the prevalence of sarcopenia and sarcopenic obesity in patients after a colorectal surgical procedure and the relationship of sarcopenia with gender-specific body composition and surgical site infections. Thereby, the microbial spectrum of SSIs of sarcopenic patients to that of SSIs of patients without sarcopenia was compared.

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Chapter 2

What determines the (in-) efficacy of a surveillance system to reduce surgical site infections after gastrointestinal surgery?

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Abstract

Aims: A surgical site infection (SSI) is a serious and costly complication with the highest rates being reported after gastrointestinal surgery. The objective of this cross sectional study was to assess the incidence and risk factors for SSIs after gastrointestinal surgery during and after hospitalisation, and to evaluate the effect of the VMS (Dutch acronym: *VeiligheidsManagementSysteem*) safety programme on the SSI rate.

Materials & methods: We assessed the SSI rate from July 2008 until December 2011, according to the criteria of the Centers for Disease Control and Prevention (CDC), before and after implementation of the VMS safety programme, which includes a bundle of four interventions. We differentiated between the SSI rate during and after hospitalisation and between superficial, deep and organ/space infections. The incidence of SSI in relation to the wound class, risk factors for SSI, and the compliance with the programme were assessed. Data were obtained during a thirty-day follow-up period after surgery.

Results: Surveillance after discharge significantly increased the overall SSI rate. An age higher than fifty years and contaminated or dirty wounds were risk factors for SSIs. Despite increased compliance with the safety programme, no significant decrease in SSI rate was found after implementation.

Conclusion: The Dutch VMS safety programme did not show a significant effect on the decrease in incidence of SSI. Surveillance, during and after hospitalisation, is essential for a reliable assessment of the SSI rate.

Introduction

A surgical site infection (SSI) is a serious and costly complication resulting in prolonged hospital stay, increased antibiotic use, increased morbidity, and even mortality [1-4]. SSIs affect up to 5% of surgical patients, with the highest rates being reported after gastrointestinal surgery [5-9]. The negative effect that SSI has on patient safety depends partly on whether the infection is superficial or deep or whether it concerns organ or space, i.e., any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure [8, 10]. Since the risk of an SSI is amongst others associated with the degree of intrinsic microbial contamination of the surgical wound, wounds are classified into four wound classes [11]. Patients with advanced stages of disease and multiple co-morbid diagnoses are often referred to a tertiary care hospital for further treatment [12]. In addition, since shorter hospitalisation after surgery has become common practice, it is to be expected that an increased number of SSIs will be diagnosed after discharge [11, 13, 14]. Surveillance of SSI is an important strategy to reduce the risk for developing an SSI [15]. It consists of registration, analysis of patients' clinical data and feedback to health care workers [11, 16-19]. In the Netherlands, hospitals currently participate in a national programme intended at improving patient safety, i.e., the patient safety programme VMS (Dutch acronym: *VeiligheidsManagementSysteem*). The programme consists of ten themes, one of which focuses on the reduction of SSI, and was developed with the aim at reducing the occurrence of preventable deaths with 50% by the end of 2012. It was initiated by the Society of Hospitals (NVZ), the Dutch Federation of University Medical Centres (NFU), and the Dutch Association of Medical Specialists and Nurses & Carers (V&VN). The theme to reduce SSI contains a bundle of four interventions. The goal is to improve the compliance with these preventive measures [20]. However, it remains uncertain which factors affect the successfulness of safety measures to reduce SSIs and whether extensive efforts result in the desired outcome, i.e., reducing SSIs. The objective of this study was to assess the incidence of SSI after gastrointestinal surgery during and after hospitalisation, and to evaluate the (in-) efficacy of the VMS safety programme, designed at an academic medical centre, on the incidence of SSI. We performed an analysis based on a logistic regression model to determine risk factors for SSIs after gastrointestinal surgery.

Methods

Study setting and patients

The study was carried out from July 2008 until December 2011 in a 715-bed tertiary care hospital in the Netherlands, the Maastricht University Medical Centre (MUMC+). The study was divided in a pre-test period and a post-test period. In the pre-test period, from July 2008 till April 2010, surveillance was only performed during hospitalisation from July 2008 till July 2009. Half way during this pre-test period, the surveillance period was extended to a follow-up period of thirty days after surgery. The postdischarge surveillance was only performed for patients visiting the outpatient clinic within the thirty days after surgery. There was no systematic follow-up of all patients over the full thirty days period. April 2010 until December 2011 was the post-test period during which the VMS safety programme had been introduced and implemented at the surgical department. The effectiveness of the VMS programme was evaluated, using the incidence of SSI as indicator parameter.

Surgical site infection

All wounds after surgery were classified into four classes: clean, clean-contaminated, contaminated or dirty. The presence of superficial, deep and organ/space SSI was assessed according to the criteria of the Centres for Disease Control and Prevention (CDC) [8]. The index-surgery was defined as the first surgical intervention in this hospital. All SSIs diagnosed within thirty days after the index-surgery were registered according to the criteria of the CDC and the Dutch PREZIES (Dutch acronym: *Preventie van Ziekenhuisinfecties door Surveillance*) national guidelines [8, 21, 22]. An infection was considered as an SSI linked to the index-surgery, unless a surgical intervention in another hospital had been performed at the same surgical site within thirty days before the index-surgery. Re-surgeries in this hospital, performed at the same surgical site and within thirty days after the index-surgery, were considered to be related to this surgery, and were therefore not included in the analysis. Surgery more than thirty days after the previous surgical intervention was registered as a new index-surgery and included in the analysis. An independent experienced infection control nurse (ICN), who was trained in the assessment of SSI, collected demographic data of the patient and clinical data of the surgical procedure over the course of the study: sex, age, wound class, elective versus urgent, admission date, date of surgery, discharge date,

readmission within the postdischarge period, presence and type of SSI, and history of previous surgery. The inter-rater reliability (IRR) was evaluated by discussing difficult cases of SSI with independent physicians and checking print outs of the database every half year. The sources of information were medical records and consultations of independent physicians. Postdischarge surveillance (PDS) was assessed by examining patients' wounds during follow-up visits at the outpatient clinic within thirty days after surgery. This surveillance method included additional surgeon notes from the outpatient medical record to pre-existing clinical data, and was validated by the PREZIES network [23].

The VMS safety programme

The VMS safety programme has been developed for Dutch hospitals. One of the ten themes includes a bundle of four interventions with the aim at reducing SSIs. The bundle was intended to reach a compliance rate of at least 90%, using the Plan-Do-Study-Act-cycle as developed by the American Institute for health care Improvement [24, 25]. The SSI rate was measured to quantify the effect of the intervention measures. The elements of the bundle are peri-operative antibiotic prophylaxis, no hair removal before surgery, normothermia, and discipline in the operating room (OR), measured as the number of door movements during surgery [24]. Concerning the PDSA cycle, in the 'Plan' phase we determined the number of surgical index-surgeries and the SSI rate during the study period. In the 'Do'- phase surveillance was performed to collect, analyse and interpret the relevant data. During the 'Study'- phase trends over time in SSI rate and risk factors were investigated. In the 'Act'-phase, the putative interventions which should be made to improve compliance with the infection prevention policy in the future, were determined.

Compliance with the VMS safety programme

Random observation of infection control practices was yearly performed at the OR for gastrointestinal procedures. This was done by infection control personnel, using a specifically developed checklist that consisted of infection control practices related to surgical and anaesthesia procedures. Monitoring at the OR was performed throughout all activities related to the same procedure. OR personnel were not notified in advance of which surgical procedures were about to be monitored. The number of door movements was measured from the start of the incision until the surgical wound was closed. Antimicrobial therapy was provided

according to the hospital-specific guidelines of the Dutch working party on Antibiotic policy (Dutch: *Stichting Werkgroep AntibioticaBeleid*, SWAB) [26]. Cefuroxime, 1500mg intravenous, or cefazoline 500 mg with 500 mg metronidazole intravenous or 2.2 gram amoxicillin-clavulanic acid intravenous for patients who underwent colorectal surgery, within 30 minutes to 1 hour before incision. Patients who underwent other laparotomies (clean procedures) did not receive antimicrobial treatments. For a morbidly obese patient two grams of a second generation cephalosporin or one gram ertapenem was more appropriate. Hair removal was omitted, if necessary a clipper was used instead. Normothermia was defined as a body temperature between 36°C and 38°C at the end of the surgery. This was achieved with intravenous fluids and a forced-air cover [27]. Between the monitoring events no specific interventions were established to improve compliance other than increasing awareness of the guidelines.

Statistical Analysis

The incidence of SSI was defined as the number of SSIs per number of surgical procedures and was calculated for the pre-test and the post-test periods. The SSI rate during hospitalisation in the post-test period was compared to that of the pre-test period, using the Pearson's chi-square test. The univariate relationship between each independent variable and SSI was evaluated using a logistic model for continuous variables. Variables with the lowest infection risk were taken as reference group (clean wounds, age less than thirty years and elective procedures). Logistic regression was performed to assess the impact of a number of factors on the likelihood that an SSI during hospitalisation in the pre-test and post-test periods occurred. The model contained ten independent variables: sex (female or male), age groups (<30 year, 30-50 year, 50-70 year or >70 year), wound classes (clean-contaminated, contaminated or dirty), previous surgery and urgency of surgery (acute or emergent). Results were considered to be significant at a *p*-value of ≤0.05. Unadjusted, adjusted odds ratios (OR) and the 95% confidence intervals (CI) were calculated for each independent variable. All statistical analysis of the data was done using the SPSS programme for Windows, PASW Statistics 18.

Results

Study population

Of the 2546 surgical procedures (including 390 re-surgeries within thirty days), 2156 index-surgeries were included in the analysis. The gender ratio was 1067 (49.5%) male and 1089 (50.5%) female. The patients' ages ranged from 18 to 98 years with a mean of 63 years for male and 62 years for female patients. Surgical procedures were classified as clean (n = 254, 11.8%), clean-contaminated (n = 857 39.7%), contaminated (n = 518, 24.0%) and dirty (n = 413, 19.2%). The wound class of 114 procedures (5.3%) was unknown. In total, 485 SSIs were diagnosed (22.5%) during and after hospitalisation, of which 243 (50.1%) were superficial, 216 deep (44.5%) and 26 organ/space (5.4%). Most superficial and deep SSIs were classified as clean-contaminated wounds (47.7% and 37.5% respectively). The organ/space SSIs were mainly classified as dirty wounds (65.4%). We observed an overall trend towards a higher incidence of SSI when progressing from clean to dirty wound procedures: 7% (clean), 24% (clean-contaminated; OR 4.0, 95% CI 2.4-6.7), 23% (contaminated; OR 1.0, 95% CI 0.7-1.2) and 32% (dirty; OR 1.6, 95% CI 1.2-2.1). For statistical analysis, 1224 surgical procedures in the pre-test period and 932 procedures in the post-test period were examined (Table I). SSI rates of contaminated and dirty wounds were significantly higher than in clean and clean-contaminated wounds, both in the pre-test as well as in the post-test period. In the post-test period patients aged fifty and higher were more likely to get an SSI. In both periods a significant longer duration of hospitalisation was found in patients with an SSI compared to those without an SSI (mean additional length of stay (LOS): 11.5 and 5.5 days respectively).

Table I: Patient characteristics with SSI and without SSI during hospitalisation, Pre-test versus Post-test

Pre-test (N=1224)				Post-test (N=932)			
Characteristics	**SSI (+)**	**SSI (-)**	**OR, 95%CI**	**Characteristics**	**SSI (+)**	**SSI (-)**	**OR, 95%CI[±]**
Number	**177 (14.5)**	**1047 (85.5)**		**Number**	**179 (19.2)**	**753 (80.8)**	
Sex			*1.30, 0.94-1.79*	**Sex**			*1.30, 0.94-1.81*
Female	81 (45.8)	547 (52.2)		Female	79 (44.1)	382 (50.7)	
Male	96 (54.2)	500 (47.8)		Male	100 (55.9)	371 (49.3)	
Age			*0.78, 0.52-1.17*	**Age**			*0.57, 0.36-0.91*
≥50	143 (80.8)	803 (76.7)		≥50	155 (86.6)	593 (78.8)	
<50	34 (19.2)	244 (23.3)		<50	24 (13.4)	160 (21.2)	
Wound class[§]			*1.54, 1.11-2.13*	**Wound class**			*1.54, 1.10-2.15*
1+2	79 (44.6)	554 (52.9)		1+2	78 (43.6)	400 (53.1)	
3+4	95 (53.7)	433 (41.4)		3+4	93 (52.0)	310 (41.2)	
Previous operation[†]			*0.84, 0.54-1.30*	**Previous operation**			*0.79, 0.52-1.22*
Yes	28 (15.8)	142 (13.6)		Yes	32 (17.8)	111 (14.7)	
No	149 (84.2)	905 (86.4)		No	147 (82.1)	642 (85.3)	
Procedure			*1.13, 0.81-1.57*	**Procedure**			*0.85, 0.61-1.18*
Emergency	63 (35.6)	402 (38.4)		Emergency	72 (40.2)	273 (36.3)	
Elective	114 (64.4)	645 (61.6)		Elective	107 (59.8)	480 (63.7)	
Hospitalisation (days)	28.9 ± 21.5	23.4 ± 29.2	*p=0.018, 95%CI 0.9-10-0*	**Hospitalisation (days)**	25.5 ± 23.7	14.0 ± 18.5	*p=0.000, 95%CI 8.3-14.7*

[±]Characteristics of patients with SSI: comparison between the Pre-test and Post-test
[§]Wound class: 1 (clean), 2 (clean-contaminated), 3 (contaminated), 4 (dirty)
[†]Previous operation within 30 days at the same surgical site

Observation of practice at the OR was performed for twenty-three randomly selected gastrointestinal surgeries. In the pre-test period the compliance rate for the four measures was less than 90%. In the post-test period a significant increase of compliance with the measures regarding antibiotic prophylaxis, shaving policy and the number of door movements was observed. No increase in compliance with normothermia measures was found. Despite this increase, compliance with measures regarding the number of door movements remained low. Overall compliance with all four preventive measures increased in the post-test period with 10% (data not shown).

Number of SSI in the Pre-test versus post-test period

The number of SSI diagnosed during hospitalisation significantly increased in time, from 14.5% in the pre-test period to 19.2% in the post-test period (OR 1.41, 95% CI 1.12-1.77, Table II). The proportion of SSIs diagnosed after discharge slightly increased in the post-test period, from 27.6% to 35.8%. The LOS of all patients (with and without an SSI) was lower in the post-test period than the pre-test period (16.2 days and 24.2 days respectively). The number of superficial SSI classified as dirty was higher in the pre-test period as compared to the post-test period (OR 5.76, 95% CI 2.92-11.34, Table III).

Results from the logistic regression analysis showed that in the pre-test period three independent variables contributed significantly to get an SSI. The strongest predictor being dirty wounds had a 23.6 times higher chance to develop an SSI than clean wounds. In the post-test period only two of the independent variables contributed significantly to get an SSI, i.e., patients older than seventy years and wounds classified as dirty. The strongest predictor for developing an SSI was again a dirty wound class which had a 4.8-fold higher risk for developing an SSI compared to clean wounds.

Table II: Patient characteristics with SSI and without SSI during hospitalisation, Pre-test versus Post-test

Pre-test Characteristics	SSI (+)	Post-test Characteristics	SSI (+)	OR, 95%-CI[‡]
Number	177 (14.5)	**Number**	179 (19.2)	*1.41, 1.12-1.77*
Superficial	88 (49.7)	Superficial	88 (49.2)	*0.98, 0.65-1.48*
Deep/Organ space	89 (50.3)	Deep/Organ space	91 (50.8)	*1.02, 0.68-1.55*
Sex		**Sex**		
Female	81 (45.8)	Female	79 (44.1)	*0.94, 0.62-1.42*
Male	96 (54.2)	Male	100 (55.9)	*1.07, 0.70-1.62*
Age		**Age**		
>70	76 (42.9)	≥70	76 (42.4)	*0.98, 0.64-1.49*
50-70	67 (37.9)	50-70	79 (44.1)	*1.30, 0.85-1.98*
30-50	26 (14.7)	30-50	21 (11.7)	*0.77, 0.42-1.43*
<30	8 (4.5)	≤30	3 (1.7)	*0.36, 0.09-1.38*
Wound class[§]		**Wound class**		
1	2 (1.1)	1	6 (3.4)	*3.03, 0.60-15.2*
2	77 (43.5)	2	72 (40.2)	*0.87, 0.57-1.33*
3	49 (27.7)	3	36 (20.1)	*0.66, 0.40-1.08*
4	46 (26.0)	4	57 (31.8)	*1.33, 0.84-2.11*
Previous operation[†]	28 (15.8)	**Previous operation**	32 (17.9)	*1.16, 066-2.02*
Emergent procedure[‡]	63 (35.6)	**Emergent procedure**	72 (40.2)	*1.22, 0.79-1.87*
Proportion PDS SSI[*]	29 (27.6)	**Proportion PDS SSI**	100 (35.8)	*1.46, 0.89-2.40*

[‡]Characteristics of patients with SSI: comparison between the Pre-test and Post-test.
[§]Wound class: 1 (clean), 2 (clean-contaminated), 3 (contaminated), 4 (dirty)
[†]Previous operation within 30 days at the same surgical site
[‡]Not elective
[*]In the Pre-test PDS was only performed from July 2009 – Apr 2010, 76 inpatient SSIs and 29 outpatient SSIs

Table III: Comparison of patients with superficial and deep/organ space SSI during hospitalisation, Pre-test versus Post-test

Pre-test			Post-test				
Variables	**Number with superficial SSI (n=88)**	**Number with deep/organ space SSI (n=89)**	**Variables**	**Number with superficial SSI (n=88)**	**Number with deep/organ space SSI (n=91)**	**OR, 95%-CI Superficial SSI**	**OR, 95%-CI[‡] Deep/Organ space SSI**
Sex			**Sex**				
Female	39 (44.3)	42 (47.2)	Female	37 (42.0)	42 (46.2)	*0.91, 0.50-1.66*	*0.96, 0.53-1.72*
Male	49 (55.7)	47 (52.8)	Male	51 (58.0)	49 (53.8)	*1.10, 0.60-1.99*	*1.04, 0.58-1.87*
Age			**Age**				
>70	41 (46.6)	35 (39.3)	≥70	38 (43.2)	38 (41.8)	*0.87, 0.48-1.58*	*1.11, 0.61-2.01*
50-70	38 (43.2)	29 (32.6)	50-70	39 (44.3)	40 (44.0)	*1.05, 0.58-1.90*	*1.62, 0.89-2.98*
30-50	7 (8.0)	19 (21.3)	30-50	11 (12.5)	10 (11.0)	*1.65, 0.61-4.48*	*0.46, 0.20-1.04*
<30	2 (2.3)	6 (6.7)	≤30	0	3 (3.3)	*0.49, 0.43-0.57*	*0.47, 0.11-1.95*
Wound class[§]			**Wound class**				
1	0	2 (2.2)	1	3 (3.4)	3 (3.3)	*0.49, 0.43-0.57*	*1.48, 0.24-9.09*
2	41 (46.6)	36 (40.4)	2	43 (48.9)	29 (31.9)	*1.10, 0.61-1.98*	*0.69, 0.37-1.27*
3	29 (33.0)	20 (22.5)	3	23 (26.1)	13 (14.3)	*0.72, 0.38-1.38*	*0.58, 0.27-1.24*
4	17 (19.3)	29 (32.6)	4	51 (58.0)	42 (46.2)	*5.76, 2.92-11.34*	*1.77, 0.97-3.25*
Previous operation[†]	14 (15.9)	14 (15.7)	**Previous operation**	11 (12.5)	21 (23.1)	*0.76, 0.32-1.77*	*1.61, 0.76-3.40*
Emergent procedure[‡]	28 (31.8)	35 (39.3)	**Emergent procedure**	33 (37.5)	39 (42.9)	*1.29, 0.69-2.40*	*1.16, 0.64-2.10*

[‡]Comparison of superficial and deep/organ space SSI between the Pre-test and Post-test.
[§]Wound class: 1 (clean), 2 (clean-contaminated), 3 (contaminated), 4 (dirty)
[†]Previous operation within 30 days at the same surgical site
[‡]Not elective

Discussion

To evaluate the factors determining the effect of the VMS safety programme on the SSI rate after gastrointestinal surgery, we compared the incidence during the pre-test period with the incidence during the post-test period. We showed that for a reliable assessment of the SSI rate, surveillance, during and after hospitalisation, is crucial. Surveillance only during hospitalisation would result in an underestimation of SSI, as in our study the SSI rate that was diagnosed after discharge increased from 27.6% in the pre-test period to 35.8% in the post-test period. We further confirmed that older age and contaminated or dirty wounds were risk factors for developing an SSI. However, despite a trend of increasing mean overall compliance with the measures of the infection preventive bundle, no association was found with a significant decrease in SSIs. Similar observations were found by others monitoring their SSI rates [28-30]. Crolla *et al.* [31] implemented a comparable safety bundle and found higher compliance rates above 60% with a significant reduction of the SSI rates by 36%. However, they used a zero-tolerance approach, a warning system for personnel who did not adhere to the prevention measures.

The safety bundle of the present study had been implemented from the second half of the pre-test period. The lowest compliance rate was observed with the number of door movements (39%). Although discipline is considered important in terms of infection control, it is difficult to measure. Therefore, we decided to count the number of door movements as being representatives for discipline at the OR. The highest compliance rate was found with the shaving measures (87%), but still not reached 90% as was the primary aim of the VMS programme. Our low overall compliance with the complete safety bundle can partly be explained by the complexity of the health care environment, the difficulty to change behaviour, and insufficient priority for infection prevention [24, 32].

The strengths of our study were the surveillance of SSI by a trained independent infection control nurse over the course of the study and the definitions of SSIs as well as the duration of the surveillance period that were defined according to the criteria of the CDC. According to the literature the assessment by an independent qualified person is the most reliable method for surveillance of SSI [33]. Correlation between the assessment by a surgical team involved in the operating procedure or the patients themselves and the infection control nurse were found to be low [33, 34].

For the postdischarge surveillance we assessed the surgical wounds during follow-up visits at the outpatient clinic. Using this "passive" PDS method the proportion of SSI diagnosed after discharge on the total percentage of SSI was 33.6%. This percentage is higher than the 14% as described by Medina *et al.* [14]. Others who used active surveillance, which not only included the results of the patients' visits to the outpatient department, but also telephone calls to the patients and the general practitioners, found percentages of postdischarge SSI up to 46% [13]. Surveillance after discharge will substantially contribute to the overall SSI rate, especially as there is an overall tendency to a decrease in hospitalisation periods resulting more often in diagnosis of an SSI after hospitalisation. However, some limitations of this study should be mentioned, that could explain the inefficacy of our surveillance system. The wound class of 114 procedures was unknown and therefore not included in the analysis. Another limitation was that some important risk factors were not included in the regression analysis, such as operative procedure, NNIS (National Nosocomial Infections Surveillance) risk index, duration of surgery and ASA-score. Instead, we used the older wound classification according to the CDC, as it also predicts the risk of SSIs based on the bacterial load at the time of the operation. We acknowledge that for a good evaluation of a surveillance method, stratification using standard risk factors is crucial to be made. Regarding our SSI rate, we only calculated an overall incidence of SSI and did not differentiate between the different surgical gastrointestinal procedures. It is to be expected that the proportion of different procedures, with different risk factors, will influence the overall incidence. Furthermore, the number of patients between the pre- and post-test differed with 24%. The lower number in the post-test period can be explained by the fact that in the post-test period patients were more intensively monitored in multidisciplinary meetings and therefore fewer patients needed to undergo an operation. Finally, the compliance with the bundle measures were based on a small number of OR observations, which might have influenced the reliability. However, it is not very likely that increasing the number of observations will result in a higher observed compliance rate. A more stringent approach (such as a zero-tolerance) is necessary to improve the compliance and to result in an improvement of patient safety.

Large variation, from 5% to 39%, in the incidence of SSI has been reported [19, 35]. Our overall SSI rate was 22.5%. Narong *et al.* found an overall SSI rate of 5.8% [36]. However, the authors missed some infections, especially in patients who were discharged early and lost to follow-up. In the study by Suljagic *et al.*, the SSI rates

ranged from 0% to 14.3% [5]. Inter-study variation is further explained by different types of hospitals a study is based on, e.g., tertiary or local community hospitals [37], and definitions of surgical site infections that are used by researchers [38-40]. Some authors diagnosed an SSI only when the bacteriological culture of the wound was positive [41], whereas we used the CDC criteria [8].

There is also variation between studies in reported incidence of SSI within the different wound classes. The National Nosocomial Infection Surveillance (NNIS) system reported an incidence of 2.1% for clean wounds, 3.3% for clean-contaminated, 6.4% for contaminated and 7.1% for dirty wounds.8 Lichtenfels *et al.* showed incidences of 1.5-2.9% for clean wounds, 2.8-7.7% for clean and clean-contaminated, 6.4-15.2% for contaminated, and 7.1-40% for dirty wounds [42]. Similar figures were also described by others [5, 43, 44]. Likewise, we found a progressively higher incidence of SSI from clean to dirty wound procedures.

In conclusion, with this study we identified factors for the (in-) efficacy of a surveillance method, as it is difficult to predict an effect on SSI after gastrointestinal surgery in our academic hospital. We tried to point out that documentation of certain important factors is required and that compliance with safety measures is ensured to consume considerable resources that might be more effectively directed to other quality initiatives. Despite a slight increase of compliance with the measures of the VMS safety programme, the number of SSI did not show a reduction over time. Also, the too short period after implementation might have contributed to the lack of observed effect. Still, interventions to improve compliance with infection prevention guidelines should be enhanced, since other studies have shown a reduction of SSI rate after bundling interventions into a programme and thereby an improvement in the compliance of health care workers [31, 45, 46]. Most important is that resources and expenditures should be well adapted according to the setting.

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Chapter 3

Microbiology of surgical site infections after gastrointestinal surgery in the south region of the Netherlands

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Abstract

Aims: To give an overview of the microbiology of blood and wound samples from surgical site infections (SSIs) after gastrointestinal surgery, as well as the antimicrobial susceptibility of the microorganisms involved, and to discuss the appropriateness of the prophylactic antibiotics administered.

Materials & methods: During a 3.5-year study period, wound swabs and blood samples of patients with an SSI were taken in the first 48 hours after surgery until 30 days thereafter.

Results: Most pathogens were isolated from wound swabs. *Escherichia coli* (25%) and *Pseudomonas aeruginosa* (10%) were the most frequently found microorganisms. Both microorganisms showed a slight tendency towards a decrease in susceptibility for the tested antibiotics, although after correction, this was not significant.

Conclusion: The comparison between wound swabs taken in the first 48 hours after a surgical procedure and swabs in the 30 days thereafter provides important information concerning the microbiology of SSIs and the development of antibiotic resistance of the causative agents over time.

Introduction

Hospital-acquired infections, also called nosocomial infections, are a frequent problem in health care facilities worldwide and contribute to longer hospital stays, prolonged periods of antimicrobial therapy, higher health care costs, higher morbidity and even mortality [1, 2]. Surgical site infections (SSIs) are one of the most frequently occurring nosocomial infections after gastrointestinal surgery, next to urinary tract, lower respiratory tract and bloodstream infections [3, 4]. Dutch hospitals aim to improve the quality of health care and patient safety by monitoring several infection control indicators and reporting incidence rates of SSI [5].

Various risk factors increase the chance of acquiring a SSI; for example, the patients' comorbidities, duration of the surgical procedure and the bacterial burden [6, 7]. Most SSIs are caused by the commensal microbiota of the patient and/or facultative anaerobic Gram-negative and Gram-positive bacteria (e.g., *Escherichia coli* and *Staphylococcus aureus*, respectively) [8–11]. Since a prolonged period of antimicrobial therapy will contribute to a higher prevalence of resistance [12], optimal antibiotic choice for prophylaxis, as well as empiric therapy, need to be based on the antibiotic susceptibility pattern of the microorganisms isolated from SSIs [13]. Apart from antimicrobial therapy, SSIs can be treated successfully by opening the wound and performing dressing changes.

In this study, we analyse the microbiological results of the wounds after gastrointestinal surgery (i.e., the microorganisms isolated from wound swabs and blood samples), as well as discussing antimicrobial susceptibility and the appropriateness of the prophylactic antibiotic choice.

Materials & methods

The study was performed from July 2008 until December 2011 in a 715-bed tertiary care hospital in the south of The Netherlands. Patients older than 18 years of age undergoing gastrointestinal surgery were included for analysis. Patients admitted with abdominal infections were excluded. The clinical data was registered by the same independent qualified infection control nurse over the course of the study. The microbiological results were retrospectively retrieved from the laboratory records at the Microbiology Department of the hospital.

Surgical site infection

An infection was considered a SSI when it occurred within thirty days after the operative procedure and no implant was left in place. All SSIs were diagnosed according to the criteria of the CDC [3]. Only index operations were included for this analysis and were defined as the first surgical intervention for a certain gastrointestinal illness in our hospital. An infection was considered as a SSI linked to the index operation unless a surgical intervention in another hospital had been performed at the same surgical site within thirty days before the index operation.

An index operation was divided into two types, elective or emergency. Elective operations were scheduled in advance with good preparation. Emergency operations were performed without delay and under acute circumstances. All wounds were classified into four wound classes depending on the type of index operation: clean wounds (non-traumatic wounds without inflammation), clean-contaminated (wound opened for drainage or reopened for other surgical reasons), contaminated (a foreign body passing through a wound) and dirty wounds (wounds exposed to faecal matter or pus) [3].

Antimicrobial therapy was prescribed according to the hospital-specific guidelines of the Dutch Working Party on Antibiotic Policy (Stichting Werkgroep AntibioticaBeleid) [14]. For the prophylaxis, either 1500 mg cefuroxime or cefazolin 1000 mg with 500 mg metronidazole intravenously was used for patients who underwent colorectal surgery, administered 30–60 min before surgery. For the empiric therapy, broad-spectrum penicillin, such as piperacillin in combination with tazobactam, was used, and in the case of severe infections, an aminoglycoside antibiotic, such as gentamicin, was added for 1–3 days. Based on culture results, the empiric therapy was adapted accordingly if necessary. Patients who underwent clean laparotomies did not receive antimicrobial treatments.

SSIs were divided into superficial (involving the skin and subcutaneous tissue), deep (involving deeper tissues of the muscle) and organ/space infections (involving organs or body spaces, outside the incision, that had been opened or manipulated during the surgery) [3].

Microbiological analysis

The inclusion criteria for the microbiological analysis were a diagnosis of SSI, a registered wound class and a wound or blood sample. Since surgical wound dressing protects primary closure incisions with sterile dressing within 48 hours

postoperatively, the wound swabs and blood samples were processed according to standard microbiological methods [15] in the first 48 hours after surgery and during the thirty days thereafter. A period of 48 h was chosen to differentiate between community- (<48 h) and hospital-acquired infections (>48 h). The swabs were either taken during surgery at the operation theatre, before the wound was closed or, in the case of an SSI during hospitalisation, at the ward.

Breakpoints for antibiotic susceptibility were determined according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing [16]. Intermediate-resistant microorganisms were considered resistant.

In the first 48 hours after surgery, we were interested in the distribution of the microorganisms between the wound classes. In the thirty days thereafter, the main focus was on the differences between the microbiological results from wound swabs and blood samples.

Results of the antibiotic susceptibility were analysed for the most frequently isolated microorganisms from wound swabs only. The prevalence of resistance to a certain antibiotic was defined as the number of antibiotic-resistant isolates divided by the total number of isolates of that species isolated from wound swabs and multiplied by 100%. To analyse the change in prevalence of resistance, we studied the microbial flora of the wound swabs taken in the first 48 hours after the operation and compared it with the microbial flora of wound swabs taken thirty days thereafter. Cultures were polymicrobial if more than one infectious agent was detected.

Statistical methods

Statistical analysis of the SSI rate, the proportion of emergency procedures and the proportion of isolated microorganisms between the wound classes were performed using binary logistic regression. The tendency in susceptibility of *E. coli* to amoxicillin/clavulanic acid, amoxicillin, cefuroxime, ciprofloxacin, gentamicin, piperacillin, piperacillin/tazobactam and cefazolin, isolated from the SSIs within the first 48 hours after surgery and those isolated after thirty days, was tested by univariable logistic regression. The same was performed for the susceptibility of *Pseudomonas aeruginosa* to ceftazidime, ciprofloxacin, gentamicin, piperacillin and piperacillin/tazobactam.

The multiple comparisons to test the susceptibility patterns of the most frequently isolated microorganisms were corrected by the false discovery rate control method. Statistical analyses were executed with SPSS software (PASW Statistics 18,

SPSS Inc., IL, USA). All tests were two-tailed and statistical significance was defined as a *p*-value <0.05.

Results

During the 3.5-year study period, the surgical department of our hospital performed 2546 gastrointestinal surgical procedures, including 390 re-operations within thirty days. The re-operations were excluded for the analysis. The actual in-hospital SSI rate was 356 out of 2156 surgical procedures (16.5%). The wound class was unknown for 114 procedures (5.3%), including 11 SSIs, and were therefore not included for further analysis. The remaining 2042 surgical procedures were classified into 254 clean (12%), 857 clean-contaminated (42%), 518 contaminated (25%) and 413 dirty (20%) procedures. The SSI rate was the highest in the clean-contaminated and the dirty procedures. Procedures classified as clean-contaminated included significantly fewer emergency ones compared with the clean procedures (odds ratio [OR]: 0.57; 95% CI: 0.43–0.76). Dirty procedures included more emergency ones (OR: 2.99; 95% CI: 2.16–4.13) (Table I).

The 345 SSIs of the 2042 procedures were classified into 171 superficial (49.6%), 155 deep (44.9%) and 19 organ/space (5.5%) SSIs. For 141 out of 345 SSI cases (40.9%), the surgical procedures were acute, and a similar proportion of procedures not resulting in a SSI was acute (41.9%; 711 out of 1697).

From 264 of the 345 SSIs (77%), wound swabs or blood samples were taken within the follow-up period of thirty days after surgery. A positive result of wound or blood during the follow-up period was found in 209 out of 264 SSIs (79%). For the other 81 SSIs (23%; mostly clean-contaminated or contaminated), other samples were taken (e.g., urine sample, drain tip or tissue of the incision) and therefore not included for the analysis.

Table I: SSI rate and the proportion of emergency procedure by wound class

	Clean (n=254)	Clean-contaminated (n=857)	Contaminated (n=518)	Dirty (n=413)
SSI				
Yes	8 (3.1%)	149 (17.4%)	85 (16.4%)	103 (24.9%)
OR 95%CI[±]	1.0 (reference)	*6.47 (3.13-13.37)*[*]	*6.04 (2.88-12.67)*[*]	*10.22 (4.88-21.38)*[*]
Surgical procedure				
Acute/emergency	105 (41.3%)	275 (32.1%)	222 (42.9%)	280 (67.8%)
OR 95%CI	1.0 (reference)	*0.57 (0.43-0.76)*[*]	*1.06 (0.88-1.44)*	*2.99 (2.16-4.13)*[*]

[±]Binary logistic regression with clean wound class as reference group
[*]=significant at p≤0.05
OR=Odds Ratio; CI=Confidence Interval

Blood samples & wound swabs in the first 48 hours after surgery

The microbiological analysis from the 264 SSIs included 96 blood samples and 168 wound swabs within the first 48 hours after surgery. Of the blood samples, 15 (15.6%) were positive from patients with different types of wounds (one clean, eight clean-contaminated, three contaminated and three dirty) and yielded 16 isolates (i.e., *E. coli* (n = 4), *Bacteroides fragilis* (n = 2) and one of each of the following species: *Candida* species, *Enterococcus faecium*, *Klebsiella oxytoca*, *Proteus mirabilis*, *P. aeruginosa*, *Enterobacter* species, *Klebsiella pneumoniae*, *Morganella morganni*, coagulase-negative staphylococci and *Staphylococcus aureus*).

Of the 168 wound swabs, 118 (70%) were positive from different types of wounds (three clean wounds, 43 clean-contaminated, 25 contaminated and 47 dirty wounds). The positive wound swabs yielded 212 isolates. The microorganisms most frequently found, irrespective of the wound class, were *E. coli* (n = 52; 25%), *B. fragilis* (n = 27; 13%), *P. aeruginosa* (n = 22; 10%) and *Enterobacter* species (n = 18; 9%), followed by a lower frequency of *E. faecalis (*n = 14; 7%), *Streptococcus* species (n = 14; 7%) and *S. aureus* (n = 11; 5%). The frequency of the isolated microorganisms did not significantly differ between the wound classes, except for

Enterobacter species with a significantly lower number in dirty wounds compared with clean-contaminated wounds (OR: 0.29; 95% CI: 0.09–0.87) (Table II).

Table II: Microorganisms isolated in the first 48 hours from positive wound swabs of 118 SSIs (n=212 isolates), per wound class

	Wound class					
Predominant MO's (n isolates)[±]	**Clean-Contaminated (n=67)**	***Rank***	**Contaminated (n=43)**	***Rank***	**Dirty (n=94)**	***Rank***
E. coli (n=52)	15/67 (22%)	*1*	10/43 (23%)	*1*	24/94 (25%)	*1*
OR; 95%CI[§]	1.0 (reference)		*1.05; 0.42-2.61*		*1.19; 0.57-2.49*	
p-value			*0.916*		*0.646*	
B. fragilis (n=27)	8/67 (12%)	*3*	7/43 (16%)	*2*	11/94 (12%)	*2*
OR; 95%CI	1.0 (reference)		*1.43; 0.48-4.29*		*0.98; 0.37-2.58*	
p-value			*0.519*		*0.963*	
Enterobacter sp. (n=18)	11/67 (16%)	*2*	2/43 (5%)	*3*	5/94 (5%)	*4*
OR; 95%CI	1.0 (reference)		*0.25; 0.05-1.18*		*0.29; 0.09-0.87*[*]	
p-value			*0.080*		*0.027*	
P. aeruginosa (n=22)	7/67 (10%)	*4*	7/43 (16%)	*2*	8/94 (9%)	*3*
OR; 95%CI	1.0 (reference)		*1.67; 0.54-5.14*		*0.80; 0.27-2.32*	
p-value			*0.374*		*0.677*	

The number of isolates in clean wounds was too low (n=8) and therefore not included in the table
[*] =significant at p≤0.05
[±] MOs with <15 isolates were not included in the table (E. faecalis (n=14), E. faecium (n=8), Streptococcus sp. (n=14), K. pneumoniae (n=7), S. aureus (n=11))
[§] Binary logistic regression with clean-contaminated wound class as reference group
Abbreviations: OR, odds ratio; 95%CI, 95% Confidence Interval; MO, microorganism

Enterobacteriaceae susceptibility pattern in the first 48 hours after surgery

The susceptibility patterns of all Enterobacteriaceae isolated from the wound swabs taken in the first 48 hours after the surgical procedure ranged from 96% for gentamicin and 94% for ciprofloxacin to 30% for amoxicillin. The susceptibility for the agents commonly used in the prophylaxis (i.e., first- and second-generation cephalosporins), cefazolin, cefuroxime and amoxicillin/clavulanic acid, was 74, 67 and 57%, respectively (Table III).

Table III: Resistant Enterobacteriaceae isolates in wound swabs in the first 48h after surgery

Antibiotic	Wound class				
	Clean (n=4)	Clean-contaminated (n=33)	Contaminated (n=16)	Dirty (n=37)	Resistance (%)
Amoxicillin	2/4	27/33	12/16	22/37	63/90 (70%)
Amoxicillin/clavulanic	2/4	19/33	10/16	8/37	39/90 (43%)
Piperacillin	1/4	13/33	6/16	12/37	32/90 (35%)
Piperacillin/tazobactam	0/4	6/33	2/16	1/37	9/90 (10%)
Tobramicin	0/4	2/33	1/16	0/37	3/90 (3%)
Gentamicin	1/4	1/33	1/16	1/37	4/90 (4%)
Ciprofloxacin	1/4	0/33	1/16	3/37	5/90 (6%)
Co-trimoxazole	2/4	5/33	2/16	9/37	18/90 (20%)
Cefazolin	2/4	11/33	5/16	5/37	23/90 (26%)
Cefuroxime	1/4	13/33	7/16	9/37	30/90 (33%)
Ceftriaxon	1/4	6/33	1/16	0/37	8/90 (9%)
Ceftazidime	1/4	5/33	1/16	0/37	7/90 (8%)

Blood samples & wound swabs from 48 hours after surgery until 30 days thereafter

Of the 264 SSIs, 117 SSIs (66%) were cultured more than once and resulted in a total of 1337 wound and blood isolates during the 30-day follow-up period. Of these isolates, 531 (39.7%) were culture-negative. In 117 SSIs (44%), the infection was polymicrobial.

Both blood samples and wound swabs were taken from 116 of the 264 SSIs (44%); from 26 of these SSIs (22%), both wound swabs and blood samples yielded a positive result, of which in almost all cases (n = 25) different microorganisms were found in the blood samples and the wound swabs. In one case, two wound swabs and two blood samples were taken and showed twice a positive sample with *E. coli* and twice a negative sample. In 56 out of the 116 SSIs (48%), *E. coli* was found in the wound swab, of which from seven SSIs (12.5%) this microorganism was also found in the blood sample. Furthermore, in 72 out of 116 SSIs (62%), the blood samples were negative whereas the wound swabs yielded a positive result, mostly with *E. coli*, *B. fragilis*, *P. aeruginosa*, *E. faecium* and *Streptococcus* species. In four out of the 116 SSIs (3%), the blood samples yielded *E. coli*, *Candida* species or coagulase-negative staphylococci, whereas the wound swabs showed no growth.

Trend in antibiotic susceptibility of E. coli & P. aeruginosa

The antibiotic susceptibilities during the follow-up period of the most frequently found microorganisms from wound swabs, *E. coli* and *P. aeruginosa,* are depicted in Tables IV & V. After correction for comparisons, *E. coli* (n = 209) slightly decreased in susceptibility during the study period for most antibiotics tested, although the decrease was not significant. Gentamicin susceptibility fluctuated at approximately 95% and ciprofloxacin at approximately 90%. After correction, a decrease in susceptibility of *P. aeruginosa* (n = 68) over time was observed for all antibiotics tested; nevertheless, no significant results were found.

Table IV: Antibiotic susceptibility of *Escherichia coli*

	First isolate[±] (N=52)	Other isolates[†] (N=157)	*p*-value	*Q*-value[§]
Amoxicillin/cluvalanic acid	37 (71%)	105 (67%)	*0.567*	*0.851*
Amoxicillin	23 (44%)	51 (32%)	*0.125*	*0.375*
Cefuroxime	44 (85%)	134 (85%)	*0.897*	*0.897*
Ciprofloxacin	47 (90%)	144 (92%)	*0.766*	*0.862*
Gentamicin	49 (94%)	146 (93%)	*0.757*	*0.973*
Piperacillin	32 (62%)	64 (41%)	*0.009*[*]	*0.081*
Piperacillin/Tazobactam	48 (92%)	129 (82%)	*0.078*	*0.351*
Co-trimoxazol	41 (79%)	109 (69%)	*0.191*	*0.344*
Cefazolin	46 (88%)	124 (79%)	*0.128*	*0.288*

[*] ***Significant at p≤0.05***
[±] ***Wound swabs cultured in the first 48 hours after the surgical procedure***
[†] ***Wound swabs cultured after the first 48 hours after the surgical procedure until 30 days thereafter***
[§] ***False Discovery Rate correction for multiple comparisons (significant at p≤0.05)***

Table V: Antibiotic susceptibility of *Pseudomonas aeruginosa*

	First isolate (N=22)[±]	Other isolates (N=46)[†]	*p*-value	*Q*-value[§]
Ceftazidime	21 (95%)	40 (87%)	*0.281*	*0.562*
Ciprofloxacin	22 (100%)	44 (96%)	*0.716*	*0.716*
Gentamicin	22 (100%)	43 (93%)	*0.512*	*0.683*
Piperacillin	22 (100%)	41 (89%)	*0.261*	*1.044*
Piperacillin/Tazobactam	22 (100%)	41 (89%)	*0.261*	*1.044*

[±] ***Wound swabs cultured in the first 48 hours after the surgical procedure***
[†] ***Wound swabs cultured after the first 48 hours after the surgical procedure until 30 days thereafter***
[§] ***False Discovery Rate correction for multiple comparisons (significant at p≤0.05)***

Discussion

For this study, we determined the prevalence of the microorganisms isolated from SSIs after gastrointestinal surgery in relation to the wound classification of the surgical procedures (i.e., clean, clean-contaminated, contaminated and dirty). In addition, we assessed the antibiotic susceptibility during a follow-up period of thirty days for the most frequently isolated microorganisms from wound swabs (i.e., *Escherichia coli* and *Pseudomonas aeruginosa*). The antibiotic susceptibility showed a decreasing tendency over time, although not significant. In all wound categories, *E. coli* was the most frequently isolated microorganism, followed by *Bacteroides fragilis* after contaminated and dirty classified procedures and *Enterobacter* species after clean-contaminated procedures. The distribution of the different species did not differ between the wound classes, except for the significantly higher number of *Enterobacter* species found in clean-contaminated wounds compared with dirty wounds. Polymicrobial results were mainly observed in SSIs after contaminated procedures.

Our most frequently isolated microorganisms are in accordance to the literature [10, 17–18]. Our low number of *Staphylococcus aureus* can be explained by the distribution of the wound types (i.e., a low number of clean wounds [12%]) in which the most common pathogen is *S. aureus*, and the highest number of clean-contaminated wounds (42%) in which *E. coli* is the most prevalent [10].

The strength of the study is that all microbiological analysis was performed in one laboratory, in contrast to others who performed the antimicrobial susceptibility testing by laboratories collaborating with the hospital, not by a central laboratory [17]. Our data were therefore not biased by differences in methodology. Moreover, data regarding the presence of SSIs were registered by the same independent qualified infection control nurse over the course of the study. In addition, in contrast to others, we investigated the wound cultures taken in the first 48 hours at the operation theatre (before the wound was closed) and compared the results with the wound cultures taken after thirty days. This allowed us to detect the decreasing tendency in antibiotic susceptibility during hospitalisation, which might be due to the use of agents for therapy if indicated (e.g., in case of spill).

Some limitations should be mentioned. In 81 cases of SSI (23%), no wound swabs or blood samples were taken and therefore not included in the bacteriological analysis. These SSIs included mostly clean-contaminated and contaminated wounds. Furthermore, we had no information regarding the antimicrobial therapy

the patients received (apart from the antimicrobial prophylaxis) for the treatment of infections during hospitalisation or after discharge. Moreover, we were unable to classify the wounds according to the National Nosocomial Infections Surveillance patient risk index, because it was not registered and therefore unknown. Instead, we used the older wound classification according to the CDC, as that also predicts the risk of SSIs. Finally, due to the low number of *P. aeruginosa* isolates, we were not able to detect a difference in the antibiotic susceptibility of this pathogen.

In 62% of the cases, the blood samples were negative whereas the wound swabs yielded a positive result, and in 3% of the cases, this was the other way around (positive blood sample and negative wound swab). These results are in accordance with the recommendations of the Expert Panel of the Surgical Infection Society and the Infectious Diseases Society of America to refrain from taking blood samples in case of a putative SSI [19].

In gastrointestinal surgery, short course antimicrobial prophylaxis is generally accepted as an effective mean to reduce the incidence of SSI [20]. The choice of the agent should be based on the microorganisms associated with the procedures performed. In our hospital, cefuroxime or cefazolin is used as a prophylactic agent and, depending on the type of surgery, in combination with metronidazole. As the antibiotic susceptibility percentages of the Gram-negative isolates of the first swabs in the first 48 hours could be used as a proxy for an effective prophylactic choice, cefazolin showed, in comparison with the other potential prophylactic agents amoxicillin/clavulanic acid and cefuroxime, the highest susceptibility of 74%. The safety of cefazolin and its favourable pharmacokinetic parameters makes this agent an appropriate prophylaxis agent [21–23]. Amoxicillin alone and in combination with clavulanic acid is widely used in our hospital, since they are active against Gram-positive and a limited range of Gram-negative organisms. Owing to the prolonged use of these antimicrobial drugs in our hospital, the resistance rate to both agents is relatively high. Some compounds, such as piperacillin/tazobactam, are given for therapy only if indicated; however, they are not generally recommended for antimicrobial prophylaxis. We do not have a clear explanation for the decrease in susceptibility to these agents. The increase in resistance to piperacillin/tazobactam might be explained by the choice of this drug in our hospital, among other reasons. The high susceptibility of *E. coli* to ciprofloxacin and gentamicin was similar to Kusachi *et al.* who found that all *E. coli* isolates in their study were susceptible to ciprofloxacin [24]. The 26–33% resistance to potential prophylactic agents is mainly due to the presence of *Enterobacter* species and *P.*

aeruginosa in the first wound swabs of the SSIs after clean-contaminated and dirty procedures.

Conclusion

To conclude, this study gives an overview of the causative pathogens of SSIs and their susceptibility patterns after gastrointestinal surgery. This information is important to guide clinicians to make an optimal empiric antimicrobial choice and it also reflects putative changes in types of pathogens isolated in SSIs.

Future perspective

The aim of this study was to examine the most common causative agents from wound swabs and blood samples of SSIs, and to guide the choice of empiric antimicrobial treatment appropriately in the case of a SSI after gastrointestinal surgery. Since the incorrect use of antibiotics will contribute to increase resistance, all efforts to optimize correct choice of empiric therapy are warranted.

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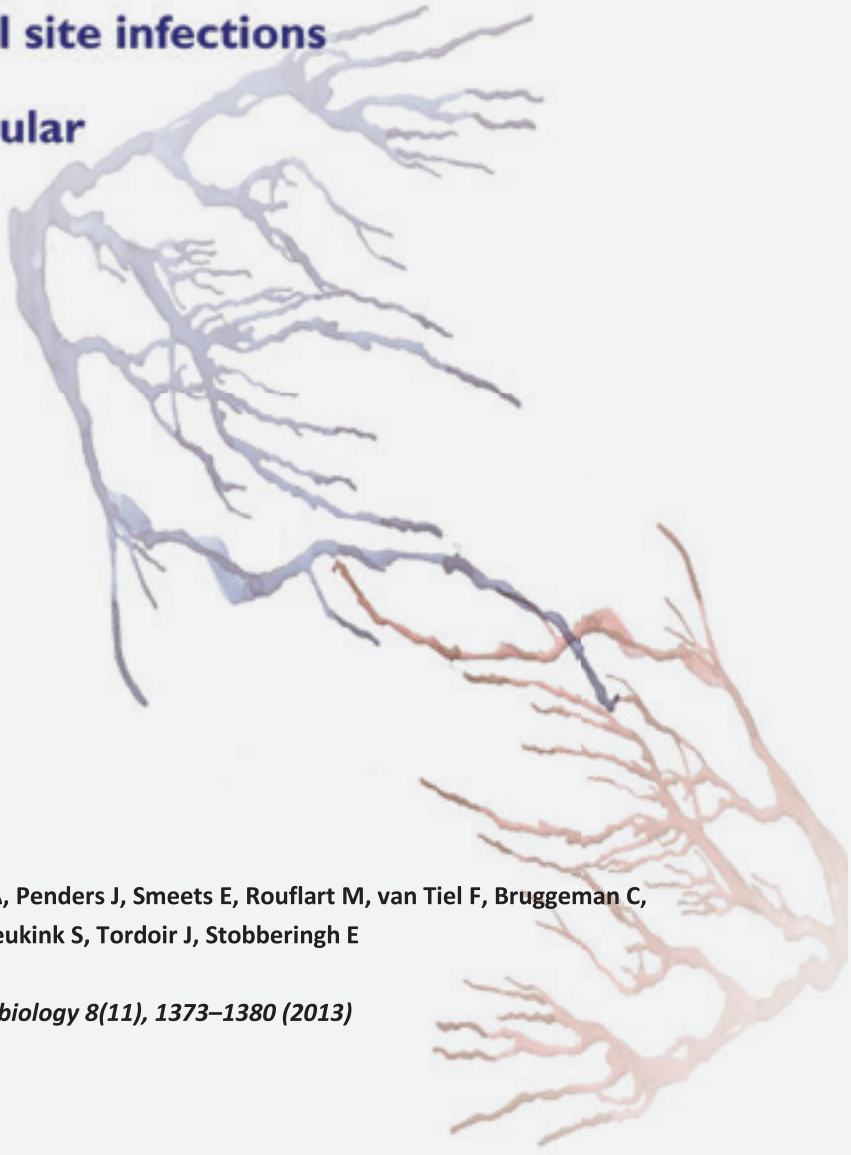
Chapter 4

A cross-sectional study on surveillance of surgical site infections after vascular surgery



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Abstract

Aims: To determine the incidence and risk factors for surgical site infections (SSI) after vascular surgery, to evaluate the Dutch safety bundle to reduce adverse complications and to analyse causative microorganisms of SSIs.

Materials & Methods: The 3.5-year study was divided into two periods: the control period (before bundle implementation) and intervention period (after implementation). Postdischarge surveillance was performed until 30 days after surgery. Causative microorganisms from in-hospital wound swabs were determined. SSI rates between both periods were compared and risk analysis was carried out by performing a logistic regression.

Results: The study included 1719 operations. The in-hospital SS rate increased significantly over time. Out of 140 SSIs, 39% were diagnosed postdischarge. Risk factors were diabetes, age >60 years and operations classified as contaminated or dirty. *Pseudomonas aeruginosa* susceptibility was the highest for gentamicin (97%). All *Staphylococcus aureus* were methicillin susceptible.

Conclusion: As patient-demographics are important to determine the effectiveness of infection preventive measures, (postdischarge) surveillance is important for developing SSI interventions.

Introduction

Surgical site infections (SSIs) after vascular surgery are serious complications, increasing the risk of morbidity, mortality and health care costs [1–3] and accounting for approximately 38% of all nosocomial infections [4]. Most vascular operations are clean, aseptic procedures, in other words, elective, not acute, nontraumatic, primarily closed and without acute inflammation. The frequency of SSI after a vascular surgical procedure ranges from less than 1 to 43% worldwide [1, 2, 5–7].

Patient-related risk factors, such as gender, older age, obesity, previous operation history, nutritional status and diabetes mellitus [1, 2, 6, 8–10], as well as operation-related factors, which include duration of operation (elective or acute) and location of incision (groin wound infection is a significant cause of postoperative complications [11]), influence the frequency of SSIs. Other factors, such as the correct use of antibiotic prophylaxis, may have an influence on the outcome. Correct use of antibiotic prophylaxis includes the correct choice of antibiotics, timing of administration and duration of treatment [9, 10, 12–14], and could prevent 40–60% of all SSIs [4, 8–11].

Although not all SSIs are preventable, many efforts have been reported worldwide to reduce the incidence of complications associated with surgery and especially SSIs [9, 15, 16]. Surveillance is an important tool to monitor the trend of SSIs. Since length of hospital stay is reduced, an increasing proportion of SSIs is diagnosed after discharge [17–21]. This proportion varies with the follow-up surveillance procedure adopted [17]; for example, active (using questionnaires or telephone interviews with patients) or passive (re-hospitalisation of patients with an SSI or follow-up visits at the outpatient clinic) [20].

From July 2010, the Maastricht University Medical Centre has been participating in the Dutch VeiligheidsManagementSystem (VMS) safety bundle to reduce adverse complications, including SSIs after surgery [48]. It has been demonstrated that optimal implementation of the program may result in a reduction of SSI [22].

We conducted a prospective cohort study to determine the incidence and risk factors for SSI after vascular surgery and evaluated the effect of the Dutch VMS safety bundle on the incidence of SSI. The most frequently isolated microorganisms involved were determined, as well as the antimicrobial susceptibility patterns of the bacteria associated with SSIs.

Materials & methods

Setting

The study was conducted at the surgical department of a 715-bed tertiary care hospital in the south of The Netherlands, the Maastricht University Medical Centre.

Dutch VMS safety bundle

The safety bundle, developed for Dutch hospitals, is a national initiative to improve surgical care by reducing postoperative complications, such as SSIs. The evidence-based measures of the bundle are preoperative antibiotic prophylaxis, no skin shaving before surgery, normothermia and hygiene discipline in the operating room, translated as the number of door movements during surgery [15, 23, 48].

The bundle was introduced and implemented by using the Plan-Do-Study-Act cycle, as developed by the American Institute for Health care Improvement [23, 49]. In the 'plan' phase we determined the incidence of SSI during the study period. In the 'do' phase, relevant surveillance data were collected, analysed and interpreted. During the 'study' phase the trend of SSI over time and risk factors for SSI, along with the causative microorganisms were investigated. In the 'act' phase, the effect of the safety bundle on the SSI rate was determined.

Timeline

The study was carried out from July 2008 to December 2011 and was divided into a control period from July 2008 to April 2010 and an intervention period from April 2010 to December 2011. From July 2008 to July 2009, surveillance was only performed during hospitalisation. Thereafter, surveillance was also performed during a 30-day follow-up period after surgery, according to the criteria of the CDC. During the intervention period, from April 2010 to December 2011, the safety bundle was introduced and implemented. The effectiveness of the bundle was evaluated, using the incidence of SSI as an indicator parameter and a risk analysis was performed for risk-factor determination. No distinction was made between types of vascular surgical procedures. Wound swabs were taken for microbiological analysis during hospitalisation and during outpatient visits if deemed necessary by the physician in charge.

Surgical site infection

All surgical procedures were classified into one of the following wound classes based on the expected bacterial load of the surgical wound: clean, clean–contaminated, contaminated or dirty, according to the criteria of the CDC and the Dutch Preventie van Ziekenhuisinfecties door Surveillance national guidelines [24, 25, 50]. The SSIs were categorized into superficial (only skin and subcutaneous tissue of the incision), deep (deep soft tissues of the incision) or anatomical infections (any part of the body that was opened during the operation, excluding the skin incision) [24].

An index operation was defined as the first surgical intervention in our hospital. All SSIs diagnosed within thirty days after the index operation were registered. An infection was considered as an SSI linked to the index surgery, unless a surgical intervention in another hospital had been performed at the same surgical site, within thirty days before the index surgery. Reoperations in our hospital, performed at the same surgical site and within thirty days after the index operation, were considered to be related to that index operation, and therefore not included in the analysis. If patients underwent surgery more than thirty days after the previous surgical intervention, this was registered as a new index operation and included in the analysis.

Demographic and clinical data of the surgical procedure, such as wound class and clinical symptoms of SSI (i.e., pain or tenderness, redness, localized warmth and swelling [50]), were collected by an experienced qualified infection control nurse over the course of the study. Other sources of information were medical records and consultations of physicians and nurses. Postdischarge surveillance to identify SSIs was conducted until thirty days following the operation during regular follow-up visits at the outpatient clinic or if the patient was re-hospitalised because of infectious complications.

Microbiological analysis

Wound swabs were processed according to standard microbiological methods [26]. Breakpoints for antibiotic susceptibility were according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing [27]. Intermediately sensitive/resistant microorganisms were considered resistant. The prevalence of microorganisms resistant to a certain antibiotic was defined as the number of antibiotic-resistant isolates divided by the total number of isolates of that species isolated from blood cultures and/or wound swabs, multiplied by 100.

Statistical analysis

The incidence of in-hospital SSI was defined as the number of SSIs per total number of surgical procedures, and was calculated for the control and intervention period separately. To compare the in-hospital SSI in the control period with the intervention period, the Pearson's chi-square test was performed. The following risk factors were determined by uni- and multi-variate analysis and stratified by study period: contamination class, history of previous operation, type of procedure (acute or elective), sex, age, diabetes mellitus, total length of stay and hospital stay before surgery.

Results were considered to be significant at a p-value of ≤0.05. All statistical analysis of the data was carried out using the SPSS programme for Windows, IBM SPSS Statistics 20 (NY, USA).

Results

Study population

During the 3.5-year study period a total of 1977 vascular surgical procedures were performed, of which 258 were reoperations within thirty days, finally resulting in 1719 index operations for the analysis. The absolute numbers of gender were 995 male (58%) and 724 female (42%). The age ranged from 22 to 98 years, with a mean of 67 years for both male and female patients.

Patient demographics & baseline characteristics

Apart from the age and number of patients undergoing acute surgery, sex, contamination of the operation, type of SSI, previous operation history, diabetes mellitus, length of stay before surgery and the hospitalisation period after surgery significantly differed between the control period and the intervention period (Table I). In the intervention period, significantly more patients had had a previous operation before the initial operation, compared with the control period.

With regard to baseline characteristics, although more operations in the intervention period were classified as clean or clean– contaminated, more infections were deep or anatomical (3.5 vs 2%; p <0.05).

Table I: Demographics of the patients and baseline characteristics in the control and the intervention period

Patient and baseline characteristics	Control period (n=857), n (%)	Intervention period (n=862), n (%)	*p*-value
Male sex	539 (63%)	456 (53%)	*<0.05*
Aged >60 years	644 (75%)	668 (77%)	*0.252*
Clean or clean-contaminated operation	688 (80%)	742 (86%)	*<0.05*
Contaminated or dirty operation	138 (16%)	106 (12%)	*<0.05*
Acute operation	243 (28%)	245 (28%)	*0.957*
Previous operation*	77 (9%)	165 (19%)	*<0.05*
Diabetes mellitus	153 (18%)	53 (6%)	*<0.05*
Length of stay before surgery (days)	7.6	3.7	*<0.05*
Hospitalisation period after surgery (days)	21.3	13.2	*<0.05*

****Previous operation in history at the same surgical site***

Infections during hospitalisation

The surgical procedures were classified as clean (n = 1402; 81.6%), clean–contaminated (n = 28; 1.6%), contaminated (n = 110; 6.4%) and dirty (n = 134; 7.8%). In 45 out of 1719 surgical cases (2.6%) the wound class was not registered and therefore unknown for the researchers.

Of all SSIs diagnosed during hospitalisation, the occurrence of deep/anatomical SSI (n = 16 + 30; 54%) was higher than superficial SSI (n = 39; 46%). When stratifying by wound classification, most of the superficial SSIs (67%) occurred after clean procedures. For all deep/anatomical SSIs, most infections (41%) were diagnosed after dirty classified procedures.

Over time, we observed an increase in the incidence of SSIs during hospitalisation from 2.8% in the control period to 7.1% in the intervention period (p <0.05; Table II).

Table II: Incidence of surgical site infections before and after implementation of the Dutch VMS bundle

Outcome measures	Control period (July 2008-April 2010)	Intervention period (April 2010-December 2011)
Number of SSI	24	61
Number of vascular index-operations	857	862
Incidence of SSI (%)	2.8	7.1
95% Confidence interval	1.9-4.1	5.5-9.0

Abbreviation: SSI, surgical site infection

Surveillance after discharge

After 1719 index operations, a total of 140 SSIs (8.1%) were diagnosed during and after hospitalisation, within the follow-up period of thirty days after surgery. During this period surveillance was also performed after discharge (from July 2009 to December 2011), 130 SSIs were diagnosed during (58%) and after (42%) hospitalisation, when visiting the outpatient clinic. Of all SSIs diagnosed after hospitalisation, 73% were superficial.

Risk-factor analysis

The results of the risk-factor analysis are shown in Table III. In the adjusted analysis, we identified an age over 60 years (OR: 2.40; 95% CI: 1.23–4.68) and an operation classified as contaminated or dirty (OR: 7.83; 95% CI: 4.71–13.01) as significant risk factors for SSI development.

Since the patient characteristics between the two study periods were noticeably different (as shown in Table I), a test was performed to investigate the interactions between all risk factors and the study period. The results showed that the interaction between diabetes mellitus and the study period was statistically significant (p = 0.005; 95% CI: 0.025–0.52). As a consequence, we performed a stratified analysis for diabetes and found that patients with diabetes mellitus had an almost threefold higher risk for acquiring an SSI, compared with patients without diabetes in the intervention group (OR: 2.99; 95% CI: 1.32–6.77), but not in the control group.

Table III: Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of SSI by risk factors

Factors	Discrete factors	SSIs/operations (n)	Unadjusted OR (95% CI)	Adjusted* OR 95% CI
Study period	Control period±	24/857	*1.0*	*1.0*
	Intervention period	61/862	*2.64 (1.63-4.28)*	*3.26 (1.94-5.47)*
Sex	Female±	33/724	*1.0*	*1.0*
	Male	52/995	*1.16 (0.74-1.81)*	*1.12 (0.70-1.79)*
Age	<60 years ±	11/407	*1.0*	*1.0*
	>60 years	74/1312	*2.15 (1.13-4.10)*	*2.40 (1.23-4.68)*
Wound class§	1+2±	45/1430	*1.0*	*1.0*
	3+4	39/244	*5.86 (3.72-9.21)*	*7.83 (4.71-13.01)*
Operation	Elective±	59/1231	*1.0*	*1.0*
	Acute	26/488	*1.12 (0.67-1.80)*	*0.59 (0.34-1.00)*
Previous operation	No±	64/1477	*1.0*	*1.0*
	Yes	21/242	*2.10 (1.26-3.50)*	*1.29 (0.74-2.24)*

Multivariate logistic regression, adjusting for the factors shown in the table (no diabetes mellitus)
±=reference group
§= 1 (clean), 2 (clean-contaminated), 3 (contaminated), 4 (dirty)
Abbreviations: OR, odds ratio; SSI, surgical site infection

Microbiology & susceptibility

Of the 85 SSIs detected during hospitalisation 44 (52%) were diagnosed after clean procedures, one (0.85%) as clean-contaminated, 14 (16%) as contaminated, and 25 (29%) as dirty wounds. The wound class was unknown for one SSI and therefore excluded for the microbiological analysis.

In 27 out of 84 SSI cases (32%), no bacteriological cultures were performed. Of the remaining 57 SSIs, 38 wound swabs (67%) were taken for microbiological analysis, of which 13 samples (34%) were considered negative as microorganisms were not isolated. From the remaining 25 wound swabs, 95 microorganisms were isolated, mainly *Pseudomonas aeruginosa* (n = 34; 36%), *Staphylococcus aureus* (n = 19; 20%), *Bacteroides fragillis* (n = 8; 8%), *Escherichia coli* (n = 8; 8%) and *Morganella morganii* (n = 7; 7%).

The antimicrobial susceptibility of *P. aeruginosa* ranged from 73.5% for ciprofloxacin to 97% for gentamicin. The susceptibility for ceftazidime and piperacillin was 88% for both antibiotics. All *S. aureus* isolates were susceptible to methicillin, the susceptibility for the other antibiotics tested ranged from 90 to 100%.

Discussion

This study was performed to determine the risk factors, incidence and microbiology of SSI after vascular surgery and to evaluate the effect of the Dutch VMS safety bundle on the incidence of SSI. In this study, our overall incidence of SSI after vascular surgery, during and after hospitalisation, was 8%. The postdischarge incidence fluctuated at approximately 4%, indicating that almost half of all SSIs were found after discharge. Most operations were classified as clean procedures. Significant risk factors for SSI were diabetes, operations classified as contaminated or dirty and an age over 60 years. Regarding the microbiology, 66% of all wound swabs (n = 38) were culture positive, with *P. aeruginosa* and *S. aureus* as the most prevalent microorganisms and the latter being methicillin susceptible.

The validity of the study was increased by the surveillance being performed by an infection-control nurse, during and after hospitalisation, over the course of the study. Performing surveillance allowed us to identify risk factors for SSI and initiate preventive interventions for the future. The addition of postdischarge surveillance up to thirty days after surgery is an important feature, as it is known that infections after vascular surgery often manifest after discharge [28, 29]. Risk-factor analysis was performed for SSIs diagnosed during hospitalisation, as risk factors for postdischarge SSIs could differ from risk factors during hospitalisation [17]. Delgado-Rodríguez *et al.* found that patients with postdischarge SSI were more similar to non-infected patients (in terms of most classic risk factors for SSI) than to patients with in-hospital SSI, diagnosed during admission [17].

Finally, all microbiological analyses were performed in one laboratory, by contrast to other studies, where the antimicrobial susceptibility testing was performed by different laboratories collaborating with the hospital and not by a central laboratory [30]. Therefore, in this study, variation due to methodological differences can be excluded.

There were, however, limitations to the study that need to be addressed. First, as we did not differentiate between the different categories of vascular surgical procedures, the results might have been inaccurately interpreted. Since SSI rates following inguinal access generally vary [2, 31], it is difficult to develop targeted interventions to prevent vascular SSIs. Second, owing to our relatively small number of microbiologically positive wound swabs, the generalizability of the microbiological results could be questioned. Third, data on The American Society of Anaesthesiologists class and length of operation as risk factors for SSI were not

retrospectively available. Instead, we used the older wound classification system according to the CDC [24], as it also predicts the risk of SSIs based on assessment of bacterial load at the time of the operation. Finally, spot checks to determine compliance with the bundle were randomly performed in the operating room. However, the number of operations was too small to draw a reliable conclusion regarding compliance with the safety bundle. Although an increasing trend in compliance was observed for the separate bundle measures (data not shown), compliance with the complete bundle was low (<50%) and showed no increasing trend over time, for which we do not have an explanation. A study by van Tiel *et al.* showed that compliance with infection-control measures can significantly improve with repeated monitoring, even with a lower number of operations for which spot-checks were performed [32]. However, van Tiel's results are difficult to compare, as with their design the contribution of individual measures to the overall outcome were identified, instead of all measures together as one complete bundle.

We were not able to demonstrate a decreasing trend in SSI after implementation of the Dutch safety bundle, but our overall SSI incidence of 8% was similar to the 5–10% found by Bandyk [31], and much lower than the 27% as described by Turtiainen *et al.* [1]. Our incidence of 4.4% (85 SSIs after 1917 surgical procedures) found during hospitalisation was also in agreement with the 4.6% described by Delgado-Rodríguez *et al.* after vascular surgery in a tertiary hospital [17]. The variation found in the literature might be due to many factors; for example, different definitions of SSI used between hospitals [33], differentiation between vascular operation types, differences in surveillance methods (leading to e.g., under-reporting in hospitals) [33–35] and hospital characteristics. Regarding the latter, higher rates of postoperative complications were observed in major teaching hospitals compared with district hospitals [7]. The failure to detect a decrease in SSI might be due to insufficient implementation of the bundle and a short evaluation period. Even successful implementations of preventive measures are not always associated with a significant decrease in SSI [15, 36–40]. Furthermore, our study population differed in demographics between the control period and the intervention period, which significantly influenced the SSI rate. Over time, more severely ill patients, some with graft infections that were diagnosed years later, were admitted to our hospital for further treatment. The changes in demographics may also contribute to the lack of decrease in SSIs.

Our study stresses the importance of postdischarge surveillance to reliably assess the incidence of SSI. During the period when postdischarge surveillance was

performed, 42% of all SSIs were diagnosed after discharge, which can be explained by our decrease in length of hospital stay [18]. Our postdischarge rate was similar to that of Delgado-Rodríguez *et al.* who found 45.6% of all SSIs after discharge [17]. Regarding the type of SSIs, more superficial infections compared with deep ones, were seen after discharge, as also found by others [41] and might be explained by the shorter hospitalisation, since superficial SSIs usually do not require antimicrobial therapy.

The results of our study confirmed the data described by others in terms of risk factors for SSI (i.e., diabetes, an age over 60 years and operations classified as contaminated or dirty). The incidence of SSI after dirty procedures is variable, both higher and lower percentages than the 18.7% we found have been described [6, 11, 29, 42, 43]. Also after clean–contaminated procedures, our incidence of SSI (3.6%) was lower than described by Tatterton and Homer-Vanniasinkam (10%) [10]. Concerning the microorganisms involved, *S. aureus* is frequently isolated [1, 10, 44, 45], whereas in our study *P. aeruginosa* was the most prevalent followed by *S. aureus*, probably owing to more patients suffering from a diabetic foot ulcer [46, 47].

Vascular operations carry significant risks due to complex surgery and long duration. As a result, the condition of the patient deteriorates. Therefore, reoperations are often necessary and a wide spectrum of antimicrobials is used. This may lead to increased antibiotic resistance, which nowadays raises concerns about antimicrobial prophylaxis practices, treatment, morbidity and mortality [15]. Information about the microorganisms involved in SSI and antibiotic resistance patterns will support an optimal choice for antibiotic prophylaxis.

Conclusion

Our study provided clinical and microbiological information on SSIs after vascular surgery. Despite evidence-based infection preventive measures, no beneficial impact was shown. Risk factors in this study, such as age of patients, diabetes and microbiological profile, must be better understood with the aim to control the frequency and morbidity associated with SSIs and to determine an optimal treatment plan. Therefore, surveillance, including postdischarge surveillance, remains important for developing timely intervention to reduce the incidence of SSI after vascular surgery in the future.

Future perspective

As vascular operations vary, for example, in complexity, SSI risk, morbidity, surgical access, duration and technique, developing new and targeted interventions to reduce SSI is difficult and should continuously be promoted and updated. Also, with rising antibiotic resistance and emerging pathogens, research should be focused on protocols providing guidelines for daily practice and (antimicrobial) treatment. All information should be based on data regarding (postdischarge) surveillance and microorganisms involved in SSI with their antibiotic susceptibility patterns.

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Chapter 5

Does sarcopenia result in a higher risk for developing surgical site infections after colorectal surgery?

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Abstract

Aims: The compromised host (immune) function of sarcopenic patients, in combination with clean-contaminated colorectal surgery, could contribute to the increased risk for surgical site infections (SSI). The aim of this study was to investigate the prevalence of sarcopenia, defined as age-related decline of muscle mass, and sarcopenic obesity in patients after a colorectal surgical procedure and the relationship of sarcopenia with gender-specific body composition and SSI. Next, to compare the microbial spectrum from SSI of sarcopenic and non-sarcopenic patients.

Materials & methods: Patients undergoing colorectal surgery in the Maastricht University Medical Center, from July 2008 to December 2011. Clinical, infectious and microbiological parameters were collected and surveillance of SSI was performed until thirty days after surgery. Sarcopenia was diagnosed by Computed Tomography imaging. SSIs were defined according to criteria of the Centers for Disease Control and prevention.

Results: There was a strong tendency towards an association between sarcopenia and SSI. Sarcopenia was significantly more common for women, aged 65 year or above, a low Body Mass Index (BMI) category (<20 kg/m^2), and patients who received peri-operative blood transfusion. Significant factors for sarcopenic obesity were male gender, aged 65 year or above, BMI category between 25.0 and 29.9 kg/m^2, former smoking behaviour, and emergent operations. In all patients with an SSI, *Escherichia coli* was the most frequently isolated microorganism, with a higher diversity of bacteria in sarcopenic patients.

Conclusion: Aging comes along with sarcopenia and a range of other independent predictors for surgical site infections. Because it is very likely that the underlying causes of sarcopenia are different in women and men, the identification of gender specific therapeutic interventions is strongly recommended.

Introduction

Ageing comprises a decrease in skeletal muscle mass and may lead to decreased strength and functionality [1, 2]. For this status, Rosenberg introduced the term 'sarcopenia' in 1989 and defined it as "*age-related loss of skeletal muscle mass and volume"* [3].

Sarcopenia is a continuous process starting at an age of 30 to 40 years. Research has shown that the average muscle strength of an 80-year old is almost half the muscle strength of a young adult2 and the prevalence of sarcopenia in this older population is over 50% [4].

Sarcopenia is negatively related to strength per unit muscle mass, also muscle quality (MQ), and is considered to be a better indicator of muscle function than strength alone5. A decrease in MQ is the result of several medical, behavioural and environmental factors that characterize the elderly [6], as well as lifestyle and behavioural changes. The (older) patient group often have nutritional problems, suffer from adverse effects of medication and changes in metabolism due to the aging process [7, 8]. In some individuals, these changes are extreme and result in a combination of substantial overweight and muscle weakness, a condition recently termed "sarcopenic obesity" [9]. The combination of sarcopenia and obesity has been shown to be a greater risk for poor health related outcomes and disability than either obesity or sarcopenia alone [10, 11].

Several methods exist to diagnose sarcopenia. Next to magnetic resonance imaging (MRI), dual energy X-ray absorptiometry (DXA) and bio-impedance analysis (BIA), computed tomography (CT) imaging is a widely used method, as it accurately quantifies the skeletal muscle mass and is an objective test of physical functioning [12].

Several studies have shown that disturbances in body composition increase the risk for complications after surgery, dependent on gender [10, 13-15]. The aim of this study was to investigate the prevalence of sarcopenia and sarcopenic obesity in patients after a colorectal surgical procedure and the relationship of sarcopenia with gender-specific body composition and surgical site infections. Next, to compare the microbial spectrum of SSIs of sarcopenic patients to that of SSIs of patients without sarcopenia.

Material & methods

This study was conducted at the surgical department of a 715-bed tertiary care University hospital, the Maastricht University Medical Center in the Netherlands.

Patient population

The study was performed from July 2008 until October 2011. The study population included patients undergoing a colorectal surgical procedure. Patients from the age of eighteen were eligible for the study if the index-operation, defined as the first colorectal surgical intervention, was performed in our hospital and if the procedure included the rectal, anal, or colonic site or creation of colonic stomata.
Ethical approval for this study was granted by the Medical Ethics committee of the Maastricht University Medical Centre.

Baseline patient characteristics

Baseline characteristics of the patients included gender, age (in years), BMI (body mass index), previous colorectal surgery, patients' comorbidities, and complications after their colorectal surgery. All complications after surgery were reported according to the Clavien-Dindo classification [16].

Computed Tomography (CT) image analysis and body composition by gender

Muscle mass was assessed by electronically stored CT images within three months prior to surgery for diagnostic and staging purposes. Patients were not consented prior to obtaining the CT image. In order to identify only the skeletal muscle area Hounsefield Unit (HU) a threshold range between -30 and 110 was used.
Our standard landmark was a transverse slice of the third lumbar vertebral level (L3), because this correlates the strongest with whole-body tissue quantities [17-19]. Two consecutive CT images extended from L3 to the iliac crest and the costae were chosen to measure muscle cross-sectional area. The L3 muscle index (cm^2) was calculated by normalizing muscle areas for length (cm^2/m^2).
Sarcopenia was defined as a L3 muscle index <41 cm^2/m^2 in women, <43 cm^2/m^2 in men with a BMI <25 and <53 cm^2/m^2 in men with a BMI >25, based on the cut-off values associated with mortality [20].
Total fat-free body mass (kg) was estimated as: 0.30 * (skeletal muscle surface area at L3 in cm^2) + 6.06 [21]. Body fat % was calculated as: (body weight (kg) – fat free body mass (kg)) / body weight (kg). Obesity was based on body fat %, with cut-off

values for obesity to be >49.6% for women and >37.5% for men, based on studies evaluating sarcopenic obesity [10, 22]. Patients were classified as obese or non-obese on the pre-operative admission date. Sarcopenic obesity was defined based on the presence of both sarcopenia and obesity.

Features associated with sarcopenia and sarcopenic obesity

Next to the clinical parameters, the influence of body composition on sarcopenia and sarcopenic obesity was tested. Sources of information were medical records and consultations of physicians and nurses. All data were obtained within the time window from the CT image until the surgical procedure.

Surgical site infections

An infection was considered a surgical site infection when it occurred within thirty days after the operative procedure if no implant was left in place or within one year if an implant was in place and the infection appeared to be related to the operative procedure [23].

Clinical data of the surgical procedure were collected prospectively by the same infection control nurse over the course of the study. To determine if sarcopenia was associated with SSI, potential predictors for SSI were selected based on the literature and availability in the patients' records. All data were obtained from medical records or retrieved after consultations of physicians and nurses. Post-discharge surveillance to identify SSIs was conducted by the same independent infection control nurse until thirty days following the operation.

Microbiology and susceptibility patterns of the surgical wounds

The microbiology of the surgical wounds of sarcopenic patients was compared to that of non-sarcopenic patients. The antibiotic susceptibility pattern was determined for the most frequently found microorganism. Breakpoints for antibiotic susceptibility were according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [24]. Intermediate resistant microorganisms were considered resistant.

Statistical analysis

To be included in the analyses, patients needed to have a CT image within three months prior to surgery. In order to detect potential selection bias, the patient group included in further analyses was compared to the excluded patients with

respect to the baseline characteristics. Body composition by gender and features associated with sarcopenia and sarcopenic obesity were determined. When parametric assumptions were met, an independent sample t-test was used for continuous variables and the Pearson's chi-square test was used for categorical characteristics.

To assess the association between sarcopenia and surgical site infections, initially the unadjusted relation was determined between sarcopenia and SSI. Subsequently, potential confounders were included in the multivariable analysis, when they change the beta-coefficient of sarcopenia by more than 5% individually. Multivariate analysis was performed after correction for confounders based on the univariate analysis. All statistical analyses were performed using the SPSS programme for Windows, IBM SPSS Statistics 20. *P*-values ≤ 0.05 were considered statistically significant.

Results

Patient population

During the study period a total of 583 patients were registered. From 321 patients (55%) CT scans were available. Baseline characteristics of the included group were compared to the remaining participants (n = 262), from whom no CT scan was available to determine the sarcopenic status. The former group was significantly older compared to the latter one. Significant differences were also observed concerning a previous colorectal operation, co-morbidities related to the gastro-intestinal tract, cardiac and renal co-morbidities. An overview of our study population is presented in Table I.

Table I: Patients with CT scan vs. patients without CT scan			
	CT % (n) (=321)	**No CT % (n) (n=262)**	***p*-value**
Male gender	56.4 (181)	57.3 (150)	*0.83*
Age (yrs) (mean, SD)	67.50 ± 12.91	58.33 ± 16.24	*0.00**
BMI (kg/m², mean, SD)	25.25 ± 4.17	25.59 ± 4.64	*0.37*
Previous colorectal surgery	11.8 (38)	19.1 (50)	*0.02**
Co-morbidities			
Diabetes	15.0 (48)	11.1 (29)	*0.17*
Hypertension	34.3 (110)	28.6 (75)	*0.15*
Hypercholesterolemia	10.0 (32)	6.5 (17)	*0.13*
Lipid deficiency	0.9 (3)	0.8 (2)	*0.82*
Pulmonary	10.0 (32)	8.4 (22)	*0.52*
Cardiac	21.5 (69)	13.4 (35)	*0.01**
PAD (Fontaine)	3.1 (10)	2.7 (7)	*0.75*
Gastro-intestinal	15.6 (50)	30.5 (80)	*0.00**
Renal	8.4 (27)	3.8 (10)	*0.02**
Hematologic disorder	0.9 (3)	1.5 (4)	*0.51*
Musculoskeletal disorder	10.9 (35)	8.8 (23)	*0.39*
Complications: Clavien-Dindo grade			
<3	71.3 (229)	77.1 (202)	*0.12*
≥3	26.8 (86)	21.8 (57)	*0.16*

* ***Significant at p≤0.05***
Abbreviations: BMI, body mass index; SD, standard deviation

Body composition by gender

Table II shows the difference between the female and male gender. First of all, men have a significantly higher weight than women (p <0.001). Furthermore, there are significant differences between men and women with regard to body fat percentage, fat free body mass, length, lumbar total muscle cross-sectional area and skeletal muscle index (all p <0.001). Men and women did not differ in overall BMI (respectively 25.6 kg/m^2 and 24.8 kg/m^2, p = 0.06). Men had a higher fat free body mass (52.1 kg vs. 38.2 kg), length (176 vs. 163 cm) and skeletal muscle index (49.5 vs. 40.1 cm^2/m^2) than women. However, women showed a higher body fat percentage (38.2% vs. 52.1%, p <0.001).

Table II: Body composition by gender

Characteristics	Men (n=181) No (%)	Women (n=140) No (%)	*p*-value
Weight, kg	*<0.001*		
Mean	81.4	68.9	
SD	11.7	13.4	
BMI, kg/m^{2†}	*0.06*		
Mean	25.6	24.8	
SD	3.7	4.7	
BMI category, kg/m^{2†}	*0.01*		
<20.0	11 (6.1)	21 (15.0)	
20.0 to 24.9	64 (35.3)	56 (40.0)	
25.0 to 29.9	77 (42.5)	37 (26.4)	
≥ 30	22 (12.2)	21 (15.0)	
Undetermined	*7 (3.9)*	*5 (3.6)*	
Body fat %			*<0.001*
Mean	33.3	40.9	
SD	9.3	9.6	
Fat-free body mass (kg)			*<0.001*
Mean	52.1	38.2	
SD	8.1	5.0	
Length, cm	*<0.001*		
Mean	176	163	
SD	6.6	7.4	
Weight loss§	*0.65*		
Mean	2.3	2.6	
SD	4.0	4.5	
CT image analysis	*<0.001*		
Lumbar total muscle cross-sectional area, cm^2			
Mean	153.4	107.1	
SD	27.1	16.8	
Skeletal muscle index, cm^2/m^2	*<0.001*		
Mean	49.5	40.1	
SD	8.7	6.2	

†BMI calculated as patient weight (kg)/length (m^2)
§Weight loss after surgery
$^{\pm}$Skeletal muscle index calculated as lumbar total muscle cross-sectional area (cm^2)/length (m^2)
Abbreviations: BMI, body mass index; CT, computed tomography; SD, standard deviation

Features associated with sarcopenia and sarcopenic-obesity

From 318 patients all data was available to determine sarcopenia. The prevalence of sarcopenia was 54%, (173 out of 318 patients). With regard to sarcopenic obesity, from 309 patients all data was available, resulting in 21% (66 out of 309) to be sarcopenic obese.

For this patient population, sarcopenia was more common in women, aged equal or above 65 year, and patients with the lowest BMI category (<20 kg/m^2). Also, more sarcopenic patients received peri-operative blood transfusion. Significant predictive factors for sarcopenic obesity were male gender, aged 65 year or above, BMI category between 25.0 and 29.9 kg/m^2, former smoking behaviour, and emergent operations (Table III).

With regard to body composition, patients with sarcopenia had a significantly lower weight and BMI compared to non-sarcopenic patients. Contrarily, sarcopenic obese patients had a significantly higher weight and BMI compared to non-sarcopenic obese patients (Table IV).

Table III: Features associated with sarcopenia and sarcopenic obesity						
Characteristic	**Sarcopenia**		***p*-value (OR; 95% CI)**	**Sarcopenic Obesity**		***p*-value (OR; 95% CI)**
	Yes n=173 (%)	**No n=145 (%)**		**Yes (n=66)**	**No (n=243)**	
Sex						
Female	86 (49.7)	54 (37.2)		13 (19.7)	122 (50.2)	
Male	87 (50.3)	91 (62.8)	*0.03 (0.60; 0.38-0.94)*	53 (80.3)	121 (49.8)	*0.00 (4.11; 2.13-7.93)*
Age, years						
<65	50 (28.9)	62 (42.8)		10 (15.2)	97 (39.9)	
≥65	123 (71.1)	83 (57.2)	*0.01 (1.84; 1.15-2.93)*	56 (84.8)	146 (60.1)	*0.00 (3.72; 1.81-7.65)*
Site of surgery						
Colon	122 (70.5)	96 (66.2)		47 (71.2)	166 (68.3)	
Rectum	51 (29.5)	49 (33.8)	*0.41 (0.82; 0.51-1.32)*	19 (28.8)	77 (31.7)	*0.65 (0.87; 0.48-1.58)*
BMI category, kg/m^{2†}						
<20.0	27 (15.6)	5 (3.4)		1 (1.5)	31 (12.8)	
20.0 to 24.9	62 (35.8)	58 (40.0)	*0.00 (0.20; 0.07-0.55)*	13 (19.7)	107 (44.0)	*0.21 (3.77; 0.47-29.93)*
25.0 to 29.9	65 (37.6)	49 (34.0)	*0.01 (0.25; 0.09-0.68)*	44 (66.7)	70 (28.8)	*0.00 (19.49; 2.57-147.88)*
≥ 30	12 (6.9)	31 (21.4)	*0.00 (0.07; 0.02-0.23)*	8 (12.1)	35 (14.4)	*0.07 (7.09; 0.84-59.89)*
Malignancy						
No	52 (30.1)	40 (27.6)		12 (18.2)	71 (29.2)	
Yes	121 (69.9)	105 (72.4)	*0.63 (0.89; 0.54-1.44)*	54 (81.8)	172 (70.8)	*0.08 (1.86; 0.94-3.68)*
Chemotherapy/radiation						
No	152 (87.9)	122 (84.1)		61 (92.4)	206 (84.8)	
Yes	21 (12.1)	23 (15.9)	*0.34 (0.73; 0.39-1.39)*	5 (7.6)	37 (15.2)	*0.11 (0.46; 0.17-1.21)*
Must score ≥2[§]						
No	108 (62.4)	108 (74.5)		47 (71.2)	169 (69.5)	
Yes	54 (31.2)	34 (23.4)	*0.07 (1.59; 0.96-2.63)*	19 (28.8)	69 (28.4)	*0.97 (0.99; 0.54-1.81)*
Undetermined	*11*	*3*		*0*	*5*	
Smoking behaviour						
Non-smoker	74 (42.8)	66 (45.5)		22 (33.3)	117 (48.1)	
Former (non-smoker >3wks)	59 (34.1)	54 (37.2)	*0.92 (0.97; 0.59-1.60)*	31 (47.0)	81 (33.3)	*0.02 (2.04; 1.10-3.77)*
Current smoker	34 (19.7)	24 (16.6)	*0.46 (1.26; 0.68-2.35)*	13 (19.7)	42 (17.3)	*0.21 (1.65; 0.76-3.56)*
Undetermined	*6*	*1*		*0*	*3*	
Diabetes						
No	148 (85.5)	122 (84.1)		52 (78.8)	209 (76.6)	
Yes	25 (14.5)	23 (15.9)	*0.73 (0.90; 0.48-1.66)*	14 (21.2)	34 (14.0)	*0.15 (1.66; 0.83-3.31)*
Type of surgery						
Laparoscopy	21 (12.1)	24 (16.6)		8 (12.1)	36 (14.8)	
Laparotomy	149 (86.1)	120 (82.8)	*0.28 (1.42; 0.75-2.67)*	58 (87.9)	207 (85.2)	*0.58 (1.26; 0.56-2.86)*
Undetermined	*3*	*1*		*0*	*0*	
Blood transfusion						
No	122 (70.5)	124 (85.5)		46 (69.7)	193 (79.4)	
Yes	51 (35.7)	21 (14.5)	*0.00 (2.47; 1.40-4.35)*	20 (30.3)	50 (20.6)	*0.10 (1.68; 0.91-3.09)*
Urgency						
Elective	94 (54.3)	87 (60.0)		30 (45.5)	145 (59.7)	
Emergency	79 (45.7)	58 (40.0)	*0.31 (1.26; 0.81-1.97)*	36 (54.5)	98 (40.3)	*0.04 (1.78; 1.03-3.07)*
Use of Prednisone						
No	162 (93.6)	140 (96.6)		61 (92.4)	233 (95.9)	
Yes	11 (6.4)	5 (3.4)	*0.24 (1.90; 0.65-5.60)*	5 (7.6)	10 (4.1)	*0.25 (1.91; 0.63-5.80)*
Operation duration, minutes (mean, SD)	183.16 ± 126.16	183.57 ± 103.19	*0.98 (1.00; 0.99-1.00)*	192.69 ± 128.76	184.42 ± 112.81	*0.61 (1.00; 0.99-1.00)*
Previous colorectal surgery	153 (88.4)	127 (87.6)		60 (90.9)	214 (88.1)	
No	20 (11.6)	18 (12.4)	*0.82 (0.92; 0.47-1.82)*	6 (9.1)	29 (11.9)	*0.52 (0.74; 0.29-1.86)*
Yes						
Nr. of patients with antibiotics≥24h	73 (42.2)	68 (46.9)		28 (42.4)	110 (45.3)	
No	33 (19.1)	26 (17.9)	*0.59 (1.18; 0.64-2.18)*	17 (25.8)	42 (17.3)	*0.19 (1.59; 0.79-3.20)*
Yes	*67*	*51*		*21*	*91*	
Undetermined						

[§]High risk for malnutrition
[†]BMI calculated as patient weight (kg)/length (m^2)
Abbreviations: BMI, body mass index; SD, standard deviation; MUST, Malnutrition Universal Screening Tool

Table IV: Influence of body composition on sarcopenia and sarcopenic obesity

Characteristics	Sarcopenia		*p*-value (OR; 95% CI)	Sarcopenic Obesity		*p*-value* (OR; 95% CI)
	Yes n=173 (%)	No n=145 (%)		Yes (n=66)	No (n=243)	
Weight, kg			*0.01 (0.98; 0.96-0.99)*			*<0.001 (1.06; 1.04-1.08)*
Mean ± SD	73.99 ± 14.77	78.38 ± 12.44		84.09 ± 10.37	73.81 ± 13.92	
BMI, kg/m^{2†}			*<0.001 (0.88; 0.83-0.93)*			*<0.001 (1.15; 1.07-1.23)*
Mean ± SD	24.30 ± 4.07	26.37 ± 4.01		27.07 ± 2.58	24.77 ± 4.38	
Body fat %			*<0.001 (1.11 ± 1.08-1.14)*			*<0.001 (1.16; 1.12-1.22)*
Mean ± SD	40.57 ± 8.65	31.97 ± 9.87		45.24 ± 5.86	34.24 ± 9.83	
Fat-free body mass (kg)			*<0.001 (0.87; 0.85-0.90)*			*0.17 (0.98; 0.95-1.01)*
Mean ± SD	41.52 ± 7.68	51.42 ± 9.49		44.61 ± 7.39	46.50 ± 10.43	
Length, cm			*0.63 (1.01; 0.98-1.03)*			*0.00 (1.05; 1.02-1.08)*
Mean ± SD	170.44 ± 9.08	170.19 ± 9.47		173.39 ± 9.17	169.49 ± 9.11	
Weight loss§			*0.46 (1.02; 0.97-1.08)*			*0.42 (1.03; 0.97-1.09)*
Mean ± SD	2.60 ± 4.37	2.24 ± 4.04		2.80 ± 4.95	2.33 ± 3.99	
CT image analysis			*<0.001*			*0.17*
Lumbar total muscle cross-sectional area, cm^2			*(0.96; 0.95-0.97)*			*(0.99; 0.99-1.00)*
Mean ± SD	118.19 ± 25.60	151.19 ± 31.65		128.51 ± 24.64	134.81 ± 34.77	
Skeletal muscle index, cm^2/m^{2‡}			*<0.001 (0.77; 0.73-0.82)*			*0.00 (0.95; 0.91-0.98)*
Mean ± SD	40.22 ± 6.08	51.80 ± 7.90		42.45 ± 5.93	46.43 ± 9.57	

** Significant at p≤0.05*
† BMI calculated as patient weight (kg)/length (m^2)
§ Weight loss after surgery
‡ Skeletal muscle index calculated as lumbar total muscle cross-sectional area (cm^2)/length (m^2)
Abbreviations: BMI, body mass index; CT, computed tomography; SD, standard deviation

Association between sarcopenia and surgical site infections

Univariate analysis determined age, gender, wound class, BMI category, chemo- or radiotherapy, type of surgery (laparotomy or laparoscopy), and operation duration as potential confounders for the association between sarcopenia and SSI. Correction for confounders showed that, although there was a tendency towards a higher risk for SSI in sarcopenic patients, the association between in this study population was not significant (p = 0.09; OR, 95% CI: 1.75, 0.93-3.32) (Table V).

Table V: Multivariate analyses for predictors of SSI			
Characteristic	**No. of patients**	**No. of SSI (%)**	***p*-value***
SMI			*0.09*
Non-sarcopenic	145	30 (20.6)	
Sarcopenic	173	43 (24.9)	
Undetermined	*3*	*0*	
Sex			*0.07*
Female	140	26 (18.6)	
Male	181	47 (26.0)	
Age, years			*0.36*
<65	114	24 (21.1)	
≥65	207	49 (23.7)	
Wound class			*0.44*
Clean	3	1	
Clean-contaminated	203	49	
Contaminated	63	11	
Dirty	39	9	
Undetermined	*13*	*3*	
BMI category, kg/m^{2†}			*0.03*
<20.0	32	2 (6.3)	
20.0 to 24.9	120	26 (21.7)	
25.0 to 29.9	114	27 (23.7)	
≥ 30	43	14 (32.6)	
Undetermined	*12*	*4*	
Chemotherapy/radiation			*<0.001*
Yes	45	23 (51.1)	
No	276	50 (18.1)	
Type of surgery			*0.09*
Laparoscopy	45	4 (8.9)	
Laparotomy	270	67 (24.8)	
Undetermined	*6*	*2*	
Operation duration, minutes (mean, SD)	190.70 ± 119.60	180.43 ± 115.12	*0.69*

Significant at p≤0.05
Abbreviations: SMI, skeletal muscle index; BMI, body mass index; SD, standard deviation

Microbiology and susceptibility patterns in sarcopenic patients with an SSI

Of all sarcopenic patients with an SSI (n = 43), 27 wounds were clean-contaminated (63%), 8 were contaminated (19%) and 8 were dirty (19%). There were no clean wounds. The most frequently found microorganism were *Escherichia coli* (20%),

followed by *Pseudomonas aeruginosa* (12%), *Bacteroides fragilis* group (8%), *Candida albicans* (8%) and *Enterococcus faecalis* (7%), independent of wound type.
In the non-sarcopenic patients with an SSI (n = 30), 1 wound was clean, 22 wounds were clean-contaminated (73%), 3 were contaminated (10%) and 1 was dirty. In 3 cases the wound class was undetermined. The most frequently isolated microorganisms were *Escherichia coli* (53%), followed by *Bacteroides fragilis* group (10%), *Enterococcus faecium* (8%) and *Morganella morganii* (3%). *E. coli* was significantly more prevalent in non-sarcopenic patients compared to sarcopenic patients (OR = 4.56, 95% CI: 2.14-9.82), but the diversity in microbial spectrum was higher in sarcopenic patients (19 different species in sarcopenic patients versus 11 different species in non-sarcopenic patients, data not shown).
Differences in the antibiotic susceptibility patterns between sarcopenic and non-sarcopenic patients were found for *E. coli* to ciprofloxacin (16.7% versus 0%, p = 0.03) and piperacillin/tazobactam (5.6% versus 30.8%, p = 0.04).

Discussion

In the present study the prevalence of sarcopenia and sarcopenic obesity in patients after a colorectal surgical procedure and the relationship of sarcopenia with gender-specific body composition and surgical site infections were determined. Also, the microbial spectrum from SSIs of sarcopenic and non-sarcopenic patients was compared.
We found that sarcopenia in patients undergoing a colorectal operation was significantly more common in women than in men, in patients aged equal or above 65 year, and in patients with the lowest BMI category (<20 kg/m^2). Also, more sarcopenic patients received peri-operative blood transfusion. Significant factors for sarcopenic obesity were male gender, aged equal or above 65 year, BMI category between 25.0 and 29.9 kg/m^2, former smoking behaviour, and emergent operations. There was a tendency towards an association between sarcopenia and surgical site infections, although not significant. With regard to the microbial spectrum, *Escherichia coli* was the most frequently isolated microorganism from SSIs from both sarcopenic and non-sarcopenic patients, an organism that is generally found in lower tract surgery [25].
To our knowledge, this is the first study that analysed the microbiology of the wounds of sarcopenic patients with an SSI, combined with the association of sarcopenia in colorectal patients with surgical site infections. The second strength

was that next to the standardization of data for length, degree of obesity, and age, standardization for gender effects was performed. It has been shown that significant gender differences in body composition were evident prior to the onset of puberty. In general, pre-pubertal girls have a higher total body fat and percentage body fat but lower fat-free mass compared to pre-pubertal boys [26, 27]. The gender differences could be explained by the sex hormones that produce different reactions in the fat metabolism. Although there was a tendency towards a higher risk for SSI in sarcopenic patients, the association was not significant after correction for potential confounders, in contrast to others who found a significant increased risk for postoperative infections in patients with sarcopenia [28]. We found a higher risk for sarcopenia in patients equal or older than 65 years, as was also found by others [11, 29, 30]. Although sarcopenic patients have a lower weight, sarcopenic obesity is associated with a higher weight. The increase in body weight is probably due to the decline in energy expenditure; decreased physical activity and reduced metabolism [31]. The lower weight in sarcopenic patients can be explained by anorexia of aging [32].

The third strength of this study is that patients were not selected to obtain a CT scan, a widely used method with high sensitivity and specificity that accurately measures a direct property of the muscle due to the high radiation exposure [1, 33, 34]. Fourth, surveillance regarding SSIs was performed prospectively by an experienced infection control nurse during the course of the study and all measurements were done by a researcher who was blinded for clinical outcome to avoid bias. Finally, all microbiological analysis was performed in one laboratory, thus excluding interlaboratory variability.

The risk for sarcopenic patients to develop SSIs can be explained by their comorbid conditions that keep the patient nutritionally impaired and/or immune-compromised. However, the loss of muscle mass might also be deemed a normal phenomenon, in contrast to other circumstances where the process is obviously increased and disease related.

Several weaknesses in our study should be addressed. First, due to the retrospective data analysis of CT images within the thirty days prior to the surgical procedure, some data could not be captured and therefore patients without an available CT image to determine sarcopenia were excluded for the analysis, which could have come along with selection bias regarding the disease status of the patient. Second, possibly due to the absence of a WHO-classification for sarcopenia and consensus on the definition and diagnosis, the prevalence of sarcopenia (70%)

in our (specific) study population with a mean age of sixty-seven years was relatively high compared to the 5-13% in the general (healthy) population of 60-70 year old people [29]. Thereby, because of the heterogeneity of populations studied throughout the literature, e.g., sarcopenic patients and muscle mass in relation to chemotherapy toxicities [35, 36], different cut-off point for sarcopenia are used and are still under debate. We assessed the best cut-off points for the definition of sarcopenia using the images at L3, related to increased morbidity and to whole-body tissue mass, corrected for gender [28]. Third, as our study population underwent different colorectal surgical procedures and different resection sites were involved [37, 38], patients had different (site-specific), risk factors, e.g., wound class, for developing an SSI [39]. Finally, we did not register data on use of medication, such as immunosuppressive drugs, of the patient.

Our findings with regard to the susceptibility pattern of *E. coli* and the diversity in microbial spectrum in sarcopenic patients can be explained by the sometimes compromised host (immune) function, e.g., due to malnutrition. Clinical malnutrition is a disorder that often coexists with infectious and inflammatory processes and environmental problems [40]. Combined with the more contaminated wounds and the different susceptibility patterns to ciprofloxacin and piperacillin/tazobactam, the higher diversity of the microbial spectrum in sarcopenic patients could be explained. The different susceptibility patterns to ciprofloxacin and piperacillin/tazobactam might be explained by the pharmacokinetic and pharmacodynamic implications that come along with the aging process.

As the analysis demonstrated a range of independent predictors of SSI alongside that of muscle loss, the reliability of the statistical association could be questioned due to confounding. This study population underwent surgery for different abdominal diseases such as colorectal cancer, IBD (inflammatory bowel disease, such as Crohn's disease and colitis ulcerosa), and diverticulitis and were thus different from the healthy elderly. Colorectal surgery remains a high-risk intervention and prognosis is multifactorial, especially in combination with sarcopenia. We underscore that it is necessary to reach a consensus on the definition of sarcopenia per clinical discipline, in order to make results from different studies comparable, particularly since study populations throughout the literature highly differ in terms of co-morbidities and medical background.

For feature research, more attention should be given to operative care, as the magnitude, duration, and consequences of postoperative complications are

determined by the complex interplay between the indication for surgery, the resulting injury of the tissue, and patient factors (e.g., age and co-morbid disease). Knowledge of the microbial agents in the wounds of sarcopenic patients with an SSI might be useful to prescribe empirical antibiotic therapy and to develop interventions for daily care of sarcopenic patients. Finally, because the likelihood is high that the underlying causes of sarcopenia are different in women and men, the identification of gender specific therapeutic interventions is strongly recommended.

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Chapter 6

General discussion & summary

General discussion and summary - Introduction

The treatment of nosocomial infections has been an increasing challenge worldwide. According to the literature, 10%–70% of nosocomial infections and 40%–60% of surgical site infections (SSIs) are preventable, depending on factors such as the study setting, study design, infection rates at baseline and type of infection [1-6]. Surveillance is an important instrument of an infection control program as the reporting of SSI rates to the surgeons reduces the rates significantly and contributes to an improvement of patient care [2, 7, 8].

Several national and international surveillance systems have been set up to monitor and control SSIs [9-14]. The Centers for Disease Control and prevention (CDC) defines surveillance of nosocomial infections as *"the on-going, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know" [*2, 15, 16]. The aims of the CDC were to develop epidemiologically sound definitions, to stratify SSI rates according to risk factors associated with the development of SSI, and to provide feedback of data [7]. In the Netherlands, SSI surveillance was set up within the national PREZIES (Dutch acronym: *PREventie van ZIEkenhuisinfecties door Surveillance*) network in 1996 [17]. They also defined surveillance according to the original definition of the CDC. The goals of PREZIES were to enable voluntarily participating hospitals to obtain insight into nosocomial infection rates, to offer benchmarking to hospitals, and to provide a basic infrastructure for further intervention research [18].

For a surveillance system to be reliable and effective in reducing SSI, it should meet the criteria, according to the Plan-Do-Study-Act cycle of the American Institute for health care Improvement [19, 20]: clear and standardised definitions, registration of clinical and laboratory data by trained and qualified infection control personnel, risk factor analysis, and feedback of data to the surgeon [2, 21, 22].

This thesis describes the evaluation of SSI surveillance in a Dutch hospital within two different patient populations, i.e., gastrointestinal (including the sarcopenic colorectal elderly patients) in **chapters 2, 3 and 5** and vascular patient groups in **chapter 4**. Our surveillance was performed before and after implementation of the Dutch VMS (Dutch acronym: *VeiligheidsManagementSysteem* [23]) safety bundle. Trends in SSI were calculated and risk factors for developing SSIs in the patient populations were analysed. We showed the importance of postdischarge

surveillance (PDS), until thirty days after surgery (without an implant), for reliable data. Furthermore, procedure-specific risk factors for SSI were observed in the different high-risk populations. However, evaluation of the VMS bundle by measuring the effect on the SSI rates showed no significant decrease in SSI over time.

Surveillance of SSI

Essential in the studies included in this thesis, was the prospective surveillance of SSI was performed by one trained independent infection control nurse. According to the literature the assessment by an independent qualified person is the most reliable method for surveillance of SSI to have a consistent interpretation of the criteria to diagnose an SSI [22, 24, 25]. Some studies have shown that lower SSI rates were found when the registration was only performed by the surgeons who are involved in the operation, compared to rates when registration was performed by an infection control nurse [25-30]. A study by Rosenthal *et al.* demonstrated an underreporting by the surgical staff of more than 50% of all SSIs during hospitalisation [27]. And a study by van Ramshorst *et al.* showed that more than 60% of all SSIs were underreported when registration of SSI was performed by surgeons [28]. On the other hand, others explained their high SSI rate by careful surveillance by a surgeon in the general surgery ward, compared to a patient's self-report through the telephone [21].

We defined SSIs based on a standard set of clinical national criteria of the Dutch nosocomial infection surveillance network PREZIES (Dutch acronym: *Preventie van Ziekenhuisinfecties door Surveillance*) and international criteria of the Centers for Disease Control and prevention (CDC) [15, 17]. For our sarcopenic patient population in **chapter 5** we assessed cut-off points to define sarcopenia, after correcting for gender differences and body compositions [31, 32].

The way surveillance is performed can be active or passive, previously mentioned in the introduction of this thesis [8]. During hospitalisation, our surveillance was active. All surgical sites were directly observed by the surgeon, and confirmed by the independent infection control nurse through review of laboratory reports, patient electronic records, and meetings with surgical personnel.

We also performed passive postdischarge surveillance (PDS), i.e., surveillance of SSI after the patient has been discharged from the hospital, until thirty days after surgery. Our overall SSI rate increased after the introduction of PDS, which

increased the reliability of the study, as well as the reliable assessment of SSIs. Our data underline the importance of PDS to avoid underestimation of the actual SSI rate [8, 33]. This is especially important since the current trends show a shortened postoperative hospital stay, more outpatient surgery, and same-day surgery [8, 34-36]. A surveillance period of thirty days after surgery (or one year when an implant is left) is recommended by PREZIES and the CDC [15, 17]. The question remains whether a follow-up period of thirty days (without an implant is left) or one year (when an implant is left) is sufficient for reliable data. Studies have shown that the onset of SSIs can occur long after a patient has been discharged [37-39]. For instance, a deep prosthetic graft infection can become manifest months to years after the operation [40].

Finally, we categorized all infections into those that affect superficial tissues (skin and subcutaneous layer) of the incision and those that affect the deeper tissues (deep incisional or anatomical) [41]. This distinction is important because deep SSIs are more severe, often require intravenous antibiotic treatment, longer hospitalisation and wound dressing. Superficial SSIs can more often be treated locally and shorter courses of oral antibiotics are generally sufficient [42-44]. Furthermore, other microorganisms are found in superficial infections compared to deeper SSIs [18, 42]. In our study, we stratified the infections according to the four different wound classes [15]. In **chapter 2**, we showed that in our gastrointestinal population 50% was superficial, 45% deep and 5% was an anatomical SSI. The superficial and deep SSIs developed largely after surgical procedures that were classified as clean-contaminated, most anatomical SSI after dirty procedures. In **chapter 4** we determined that in the vascular population most SSIs were deep/anatomical SSIs (54%) and most frequently developed after procedures classified as dirty (41%). Most superficial SSIs (67%) occurred after clean procedures. Ortega *et al. [*45] also stratified by wound class and found most superficial SSIs occurred after clean-contaminated procedures, most deep SSIs after clean procedures, and most of the organ/space SSIs also after clean-contaminated procedures.

Some authors state that the diagnosis of superficial SSI is subjective and inconsistent and are the cause of the wide range of reported SSI rate throughout the literature [25, 46, 47]. Therefore, others have suggested excluding superficial SSIs from reporting altogether, because data related to superficial SSIs would be subjective, inconsistent and therefore uncertain [41, 48]. Yokoe *et al.* , who studied patients after, amongst others, coronary artery bypass graft procedures,

questioned the lower sensitivity of superficial SSIs compared to the more complex SSIs [49]. Generally, the hospitalisation period of patients with superficial SSIs is brief, and they are readmitted less frequently compared to the patients with deep SSIs. The Efficiency of routine surveillance could therefore be limited. Instead, Kao *et al.* concluded that superficial SSIs after colon resections are a reliable indicator of hospital quality when the number of cases is acceptable [50]. However, it could be questioned if the reliability of the superficial SSI rate could become underestimated.

Our surveillance method has several limitations. First, our PDS method was passively performed instead of actively, meaning that the diagnosis of surgical wounds were based on laboratory results during follow-up visits at the outpatient clinic and electronic patient records by the infection control nurse. However, several studies have shown that not all patients visit the out-patient [51]. However, we chose this method because active PDS would have been more time-consuming and might have resulted in higher costs [52]. Other passive surveillance methods described in the literature are questionnaires sent to the patient or surgeon, or telephone interviews with patients by health care personnel. We did not choose for these methods, because not all questionnaires are returned, resulting in an underreporting of the SSI rate [51]. Also, due to time constraints, it might have been performed by others than our infection control nurse and thus have led to misclassification [35, 52]. Additionally, it was shown that reporting by the surgeon is more efficient and reliable than reporting by the patient when using a questionnaire or a telephone interview by infection control personnel [39, 53, 54]. Second, for our risk analysis we did not differentiate between the three types of SSI separately. Similar to the methods used in several other studies of SSI, superficial, deep and anatomical SSI are combined together when analysing the risk factors [55-58]. In contrast, there are also studies that compared risk factors for the types of SSI. For instance, Lawson *et al.* found a variation in superficial and deep or anatomical risk factors for SSI [42]. Blumetti *et al.* found that Body Mass Index and creation of ostomy were associated with incisional SSI and that peri-operative transfusion and previous abdominal surgery were associated with anatomical SSI [59]. Ho *et al.* also found surgical outcomes and risks for SSI to be different by infection type [60].

In conclusion, the surveillance we performed has several strengths and limitations. The registration of SSI by one and the same experienced infection control nurse is an important strength. The inclusion of PDS is a strength, but as we used only a

passive registration, this might be considered as a limitation. Also, the lack of compliance measurements with the VMS bundle is unfortunately a limitation.

SSI rates during and after hospitalisation

A reduction of SSI will result in significant advantages in terms of patient quality of life and reduced use of medical treatment. Therefore, we determined the SSI rates in different study populations during and after hospitalisation. For SSI rates to be reliable, a sufficient number of surgical procedures have to be evaluated [50]. With regard to our gastrointestinal patient population in **chapter 2**, 485 SSIs out of 2156 index operations (22.5%) were diagnosed during the follow-up period of thirty days after surgery. In the literature, SSI rates between (including postdischarge surveillance) less than 1% and more than 40% are found. Narong *et al.* assessed an overall lower SSI rate of 5.8% in this patient group [61]. However, the authors did not include all infections; especially SSIs of patients who were discharged early and lost to follow-up were missed. Also, the National Nosocomial Infections Surveillance (NNIS) System reported lower rates after gastrointestinal surgery, i.e., between 0.67% and 11.3%. Moro *et al. [*62] mentioned percentages up to 13.5%. Although Suljagic *et al.* did not conduct postdischarge surveillance to detect SSIs, they reported a percentage of 44% after abdominal surgical procedures [63]. The variation in SSI rates depends on the surgical procedure, risk factors for SSIs, and surveillance. Several studies have identified different independent risk factors for developing SSI, including different patient characteristics and other health care associated risk factors [56, 64-70].

Using PDS, 36% of all gastrointestinal SSIs were found after discharge, which was higher than the 14% as described by Medina *et al.* [71]. The difference might be explained by difference in (PDS) surveillance method. In their study, only patients were included who returned to their surgeon with a wound infection, assuming that if they did not come back the wound was healing. On the other hand, Tanner *et al.* found 41% of their total number of SSI after discharge. Although they also used a follow-up period of thirty days, they used an active method for the PDS surveillance, i.e., by telephone interviews and home visits [72].

Also for vascular surgery a great variation in the rates between studies of SSI has been found. In **chapter 4**, our overall SSI rate was 8%, which was similar to the 5-10% found by Bandyk *et al. [*56], but much lower than the 27% as described by Turtiainen *et al. [*73]. Their high rate can be explained by their diagnosis of SSI as an

infection if there were signs of infection irrespective of the culture results. The NNIS System reported low rates between 0.9 and 4.3% [10], Suljagic *et al.* found rates between 2.6% and 23.5% [63], and Moro *et al.* up to 5.4% [62]. Regarding PDS, almost half of all our vascular SSIs were found after discharge, similar to the proportion found by other investigators [74]. Our infection rate was lower than the 61% by Mannien *et al.* [55]. However, they included different types of procedures and they used a longer follow-up period of 42 postoperative days.

In our sarcopenic elderly patients in **chapter 5**, we found an overall SSI rate of 23%. The literature with regard to the association between sarcopenia and SSI is limited. However, the study by Lieffers *et al.* [31]. found the same percentage of SSI (23.7%) as in our study.

Besides the surveillance methods used, other factors might explain the large variation in SSI rate. This may be accounted for by the experience of the surgeon in charge, type of hospital, i.e., types of surgical procedures and patient case-mix, the surveillance method used, and follow-up period [10, 75-79]. The variation in follow-up period between "only during hospitalisation" up to 90 days postoperatively or even longer has been described and makes the comparsion of the results even more difficult. As previously mentioned we followed our patients until thirty days after surgery, according to the criteria of the CDC. Whereas some studies only follow their patients during hospitalisation [80, 81], others maintain longer follow-up periods of four to six weeks [29, 82, 83], or up to ninety days postoperatively, also when no implant is left at the surgical site [37]. Occasionally, the follow-up period is not mentioned at all [84].

The skills of the surgeon in charge can also influence the risk of developing an SSI [70]. Wurtz *et al.* explained the increase in the overall SSI rates by the longer operating times and less technical skill among recently qualified surgeons [85]. Castro *et al.* showed a 4.5 times higher risk of SSI for surgeons who have less than 5 year experience, compared to surgeons with more than 10 year surgical experience [86]. The variation in SSI rates throughout the literature can further be explained by the type of hospital, the complexity of operation types or the patient case-mix with different risk factors. In this regard, it is known that post-operative complications are more often observed in major teaching hospitals compared to smaller district institutions [87, 88]. Patients with advanced stages of disease and multiple co-morbid diagnoses are often referred to an academic hospital for further treatment [89]. Increased admissions of severely ill patients to our hospital over time may have occurred. Also, higher rates of health care-associated infections have been

demonstrated in tertiary referral hospitals, such as academic hospitals, compared to primary or secondary health care centres [90].
In conclusion, several factors play a role in the variation between SSI rates in the literature compared to our results. Variations in method of registration, patient case-mix, experience of the surgeon in charge, type of operation, are among others relevant to explain the difference in SSI rates.

Risk factors for SSI

Risk factors for developing SSIs depend in part on the differences in patient case mix. Between hospitals, different surgical procedures are performed. Some are more complex or more urgent than the other. As patients carry different risks for developing surgical site infections, correcting for these differences is required to allow a reliable comparison between different surgical patient populations and hospitals [91-94].
This thesis discusses non-modifiable and modifiable risk factors, some are patient-related, while others are surgery- or environment-related [95, 96]. We corrected for different risk factors or other potential factors for SSI in all patient groups, i.e., gender, age, wound classification, previous surgery and urgency of surgery, which are frequently found factors in the literature [59, 67, 69, 97].
In our gastrointestinal study population in **chapter 2**, older age and contaminated or dirty wounds were significant risk factors for developing an SSI. These risk factors were also found by others [66, 70, 97-99].
For our vascular population in **chapter 4**, we additionally corrected for diabetes mellitus, total length of stay (LOS) and hospital stay before surgery [100-104]. The risk factor analysis was only performed for SSIs diagnosed during hospitalisation, because risk factors for postdischarge SSIs can differ from risk factors during hospitalisation as shown by Delgado-Rodriguez *et al [*105]. They found variables as emergency operation, duration of operation, type of surgical wound, wound drainage, need of admission to the intensive care, and administration of antibiotics according to written protocols associated with an increased in-hospital SSI risk. But none of the variables was associated with an increased risk of SSI after discharge. Significant risk factors for in-hospital SSI in our vascular study population were diabetes, operations classified as contaminated or dirty and an age over 60 years, similar to what other authors found [74, 100, 105-107].

For our sarcopenic patient group in **chapter 5**, we also corrected for BMI category, chemo- or radiotherapy, type of surgery (laparotomy or laparoscopy), and operation duration [108-111]. In patients with sarcopenia, the risk of SSIs can be explained by their comorbid conditions that keep the patient nutritionally impaired and/or immune-compromised. To find an association of sarcopenia and the development of SSIs, we standardized for length, degree of obesity, age, and gender effects in body composition. We found a higher risk of sarcopenia in patients 65 years of age or older. Although we showed a tendency towards a higher risk of SSI in sarcopenic patients, the association was not significant after correction for potential confounders. These results are in contrast to the study of Lieffers *et al.*, describing a significant association between sarcopenia and postoperative infections [31]. Reasons for this can be different diagnostic methods, different methods of infection registration and/or different surveillance methods between both studies.

The risk factors we found in our patient populations were in part in accordance with those described in the literature [61, 64-66, 70, 107, 112-114]. However, a limitation of our risk factor analysis was the proportion of different procedures, with different risk factors, which might have influenced the trends of SSI rates. Furthermore, we were not able to gather data on The American Society of Anaesthesiologists (ASA) class and length of operation as risk factors for SSI for the risk analysis. Instead, we used the older wound classification system, i.e., clean, clean-contaminated, contaminated or dirty wound class, according to the CDC [15], because it also predicts the risk of SSIs based on the estimation of bacterial load in proximity to the wound area at the time of the operation.

The VMS safety bundle

Many interventions to prevent health care-associated infections that were implemented as a bundle have been shown to reduce infection rates [115-124]. The Dutch VMS safety bundle has been implemented at the surgical department of our hospital. In **chapters 2 and 4**, no decrease in SSIs was determined after the implementation. Similar observations were found by others monitoring their SSI rates [125-130]. On the other hand, Crolla *et al.* implemented a similar safety bundle and observed compliance rates above 60% with a zero-tolerance approach and a significant reduction of the SSI rate by 36% [131]. Hedrick *et al.* demonstrated a reduction of post-operative morbidity in patients undergoing

colorectal operations after implementation of an active surveillance system and a multidisciplinary wound-management protocol [132].

To demonstrate and up-ward step change of compliance, regularly repeated measurements of compliance would have been required. We did not observe the compliance with the VMS safety bundle on a frequent basis. Although overall compliance with the entire bundle was measured as being above 80% (data not shown), overall compliance never reached 100% during the study period. Studies have shown that compliance with infection preventive measures reduces infection rates [133]. This was also observed by Van der Slegt *et al.,* who showed that the implementation of a bundle of care was associated with improved compliance over time and a 51% reduction of the SSI-rate in vascular procedures [134]. Their findings were based on the measurements of bundle adherence every three months. Also, the results of the compliance with the bundle were communicated to all surgical personnel every three months.

Additionally, a too short evaluation period of one year of the measures might be reasons for our non-decreasing SSI rate. Furthermore, gradual change in patient-mix, lack of awareness or knowledge of the bundle by health care personnel can account for an insufficient implementation. To increase knowledge and responsibility regarding the safety bundle, communication, understanding and collaboration between researchers and health care personnel is crucial [135]. It has also been described that the bundle is not tailored well enough to the needs and working strategies of the health care personnel and setting [136].

Thus, due to several factors, our implementation of the VMS bundle has several limitations. Inadequate frequency of compliance measurement with the bundle, a too short evaluation period, and no differentiation between the different surgical procedures, are by far the most important ones. As a result, the information for optimal feedback was incomplete.

Microbiology of SSI

It has been demonstrated that the involvement of the microbiology laboratory can be useful to control the incidence of SSI, to guide prescription of antibiotics and to limit the spread of antibiotic resistant pathogens [137-140]. Therefore, we included the results of wound and blood samples during our surveillance in **chapters 3, 4 and 5** [139]. In our gastrointestinal patient population, culture results of wound swabs taken in the first forty-eight hours after the surgical procedure, were

compared with the culture results of the wound swabs taken within thirty days after surgery. This allowed us to observe which changes in antibiotic susceptibility during hospitalisation occurred. By examining the culture results in the first forty-eight hours, we were able to determine the antibiotic resistance of the empiric antibiotic treatment at time of surgery. We only reported results from wound samples, since blood samples do not add relevant information in this regard [141]. The number of (positive) blood samples (n = 15) was low [142]. In 62% of the cases, the blood samples were negative whereas the wound swabs yielded a positive result.

During hospitalisation, antibiotics are often part of the treatment, and can be used both for prophylaxis and therapy. As antibiotic use is the main risk factor for antibiotic resistance, it is to be expected that an increases in resistance will be observed [143-149]. However, no significant increase in resistance to the antibiotics tested was found for the most frequently isolated microorganisms, i.e., *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus,* in our gastrointestinal and vascular patient population. With regard to the microbial spectrum of our colorectal sarcopenic study population, *Escherichia coli* was the most frequently isolated microorganism from SSIs in both sarcopenic and non-sarcopenic patients. The National Health care Safety Network (NHSN) and others found similar microorganisms associated with SSI cases after these types of surgery [137, 150, 151].

Differences in pathogens and antibiotic resistance patterns can be explained by several factors. Although some studies diagnosed an SSI only when the bacteriological culture of the wound was positive [152], our SSI diagnosis was based on the CDC criteria, also when the culture was negative [15]. Furthermore, all our microbiological analyses were performed in one laboratory. This is in contrast to other studies, where the antimicrobial susceptibility testing was performed by different laboratories collaborating with the hospital and not by a central laboratory [150]. Therefore, variation due to methodological differences in our study can be excluded.

To conclude, the distribution of the microorganisms isolated from SSIs can vary between different patient populations, as shown in **chapters 3, 4** and **5**. Collaboration with clinical laboratory staff is crucial to gather information about the isolated pathogens and antibiotic resistance patterns. This may guide the treatment for a surgical patient, in order to prevent SSI and the occurrence of resistant pathogens.

Future directions

The prevention of surgical site infections is important for health care services, and more importantly for the patient. Methods of infection registration are therefore crucial to be evaluated. Fortunately, a significant number of SSIs is preventable. The Dutch VMS safety bundle has been implemented in our hospital with the aim to reduce SSIs, based on consistent and evidence-based measures of the bundle. For a bundle of infection preventive measures to be a useful tool for a safer operating environment, several aspects should be kept in mind and determined in order to analyse and disseminate surveillance results: the aetiology and severity of infections, high-risk populations and surgical procedures, goals of the surveillance system, standard definitions, the registration period, and appropriate personnel and tools for data collection.

Although this thesis demonstrated the importance of SSI surveillance (active and passive, during and after hospitalisation), we were not able to find a significant decrease of our SSI rate after the implementation of the VMS bundle. As discussed earlier, during the study period we have dealt with several implementation issues. In future studies, these issues should be evaluated according to the PDSA-cycle, i.e., a step-wise approach to successfully implement an intervention. Next, surveillance should be carried out according to the guidelines and all surgical staff should be involved by providing feedback of the results.

Feedback of infection rates to the involved health care professionals is highly important, because behaviour at the operating theatre is a risk factor for developing SSIs [153-155]. As already mentioned, studies have shown that compliance with infection preventive measures is not always optimal and needs to be improved in the future [156, 157]. We believe that feedback may substantially affect behaviour and enables personnel to comply with the guidelines. A tool to change behaviour is education provided to the clinical team on the one hand, and the infection control team on the other. Teamwork and continuous verbal and electronic communication are critical for effective clinical care. The compliance with the bundle measures should intermittently be monitored. Unfortunately, we were unable to find an increase in compliance rate in our studies. Furthermore, to compare SSI results between reported studies, it should be ensured that the same and concise definitions have been used and the same guidelines have been followed, with regard to the diagnosis of SSIs. But also the patient population or medical condition is important. For sarcopenic patients, there is still no consensus

about the skeletal muscle cut-off points, at which the condition is diagnosed. Therefore, we decided to calculate our own cut-off points for this particular colorectal population. However, these values cannot be used as a gold standard. Therefore, more research should be performed to diagnose sarcopenia in the aging population with different medical backgrounds. The results of studies to sarcopenia should provide further information for treatment options in order to reach the desired goals in this patient population.

Besides unambiguous definitions, the addition of microbiological analysis is also important, because the occurrence of resistant bacteria is increasing, among others by the prolonged and wide-spread use of antimicrobial prophylaxis and broad-spectrum antibiotics [158]. As our sample size of the wound cultures was small, larger sample sizes should be included in the overall surveillance method. It is of great importance to identify the causative pathogens to discuss the type of surgical antimicrobial prophylaxis and to better handle therapeutic implications. To achieve this, clinical departments must implement adequate procedures for the collection and transport of samples to the laboratory and collaboration between the infection control team, the surgical team and the microbiologists should be optimal for analysis and feedback of surveillance data.

Finally, we have shown that variation in case mix, underlying disease and severity of illness at participating hospitals should be controlled for statistical analysis. Within our study populations significant risks for developing SSIs were found due to the long duration of the surgical procedure, different types of wounds and SSIs, and complex diseases, as also found by other others. Additionally, we are an academic hospital and we were more confronted with referral patients and medical backgrounds, compared to smaller district hospitals. Throughout the literature, many risk factors for SSIs have been identified that can be used individually or in combination as scoring indices. As it is already mentioned that several studies still show that an optimal risk score for all surgical procedures is difficult to quantify, more research should be performed to identify risk factors for SSI in different patient groups with different medical conditions.

To conclude, this manuscript describes elements for an accurate infection registration method. SSIs acquired after surgery may be serious and, in some cases, life threatening. These may result in higher morbidity and adversely affect recovery. Infections may be caused by organisms resistant to antibiotics. It is therefore important that clear information on the standards of infection prevention and control in hospitals is combined and easily available to allow

adequate surveillance and to improve the quality of care. For the prevention and control of SSI, and a successful implementation of a safety bundle, a multidisciplinary approach is crucial. Activities based on infection prevention protocols should be imbedded in every day practices and adhered to by all health care workers. Through feedback they have to be made aware of the consequences for the patient when guidelines are not recognised and followed accurately. Besides the availability of tools, education, communication and support, leadership and active involvement are important aspects. We believe that the first steps in SSI prevention are the willingness, collaboration, and efforts to improve compliance with infection preventive measures. After all: an ounce of prevention is worth a pound of care!

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Samenvatting

De laatste jaren wordt in steeds meer zorginstellingen aandacht besteed aan infectiepreventie en patiëntveiligheid. Een van de redenen is de toenemende antibiotica resistentie van bacteriën waardoor infecties steeds moeilijker te behandelen zijn. Ziekenhuisinfecties ontstaan tijdens het verblijf van een patiënt in het ziekenhuis en worden ook wel nosocomiale infecties genoemd. Infecties die binnen 48 uur na opname ontstaan, worden niet gedefinieerd als ziekenhuisinfectie, omdat deze waarschijnlijk niet geassocieerd zijn aan de betreffende opname. Ziekenhuisinfecties komen in alle ziekenhuizen voor en worden meestal veroorzaakt door bacteriën die de patiënt zelf bij zich draagt of die door anderen worden overgedragen. Ze zijn doorgaans onvermijdbaar, maar de mate waarin ze voorkomen verschilt per ziekenhuis, per specialisme en per ingreep.
Voor patiënten die een operatie ondergaan zijn postoperatieve wondinfecties (POWI's) de meest voorkomende ziekenhuisinfecties en maken ongeveer 17% uit van alle ziekenhuisinfecties. POWI's zijn infecties die voorkomen binnen 30 dagen na een chirurgische ingreep of binnen één jaar na de operatie wanneer een implantaat is achtergelaten. Andere veel voorkomende infecties zijn urineweginfecties, bloedstroominfecties, pneumonie, gastro-intestinale infecties en infecties van het centrale zenuwstelsel. De literatuur beschrijft verschillende preventieve maatregelen om het aantal ziekenhuisinfecties terug te dringen.

In dit proefschrift wordt het voorkomen, de risicofactoren en het effect van infectiepreventie maatregelen op het voorkomen van POWI's na verschillende chirurgische ingrepen beschreven. Een POWI is in dit onderzoek gedefinieerd volgens de criteria van het landelijk PREZIES netwerk en de CDC.
Een algemene introductie over ziekenhuisinfecties, infectiepreventie en daaraan gerelateerde onderwerpen wordt beschreven in **hoofdstuk 1.** De surveillance van POWI's in een academisch ziekenhuis voor verschillende onderzoekspopulaties, namelijk een patiëntengroep na een gastro-intestinale ingreep (inclusief de colorectale sarcopene ouderen), wordt beschreven in de **hoofdstukken 2, 3** en **5**. In **hoofdstuk 4** wordt het voorkomen van POWI's na een vasculaire ingreep weergegeven. Tenslotte worden de resultaten in **hoofdstuk 6** bediscussieerd en worden de belangrijkste bevindingen samengevat en suggesties gegeven voor toekomstig onderzoek.

Veiligheids Management Systeem

Surveillance is een belangrijk onderdeel van een infectiepreventie programma. Verschillende studies hebben aangetoond dat feedback van infectiepercentages aan behandelaars bijdraagt aan het verminderen van het aantal wondinfecties en zodoende bijdraagt aan de verbetering van de patiëntveiligheid. Nationale en internationale surveillance-systemen zijn opgezet om het voorkomen van het aantal POWI's te registreren en zo mogelijk te verminderen. In Nederland is het VeiligheidsManagementSysteem (VMS) geïntroduceerd voor Nederlandse ziekenhuizen, met het doel het aantal vermijdbare ziekenhuisinfecties met 50% te verlagen. Het veiligheidsprogramma bevat verschillende thema's waarvan één is gericht op het voorkomen van POWI's na een operatie, ook wel de POWI interventiebundel genoemd. De bundel bestaat uit vier maatregelen: het achterwege laten van preoperatief ontharen, adequate timing, dosering en keuze van antibiotica profylaxe, beperking van in- en uitloop op de operatie kamer en perioperatieve normothermie (handhaving van de juiste lichaamstemperatuur tijdens een operatie). Om inzicht te krijgen in de naleving van deze maatregelen werd het aantal POWI's vóór en na implementatie van de VMS bundel geregistreerd. Voor dit manuscript resulteerde implementatie van de VMS bundel niet tot een significante daling in percentage postoperatieve wondinfecties tijdens de studieperiode. Mogelijke redenen hiervoor zijn dat de naleving van de maatregelen van de bundel alleen eenmalig is gemeten, de evaluatie periode te kort was en dat de patiëntengroepen verschilden in onderliggend lijden. Bovendien is geen onderscheid gemaakt in de verschillende operatieve procedures en de verschillen in complexiteit ervan.

Surveillance tijdens opname en na ontslag

Door de afname van het aantal opnamedagen na een operatie manifesteren POWI's zich steeds vaker nadat de patiënt ontslagen is uit het ziekenhuis. Het is daarom van essentieel belang dat, ook nadat de patiënt ontslagen is uit het ziekenhuis, het optreden van een infectie, gerelateerd aan de ingreep, in kaart wordt gebracht. Dit om een onderschatting van het aantal ziekenhuisinfecties te voorkomen. Onze surveillance, tijdens en na opname, van POWI's werd vóór en na implementatie van de VMS bundel uitgevoerd en geëvalueerd. De trends in POWI percentages werden berekend, risicofactoren voor het ontwikkelen van POWI's in

de verschillende patiënten populaties werden geanalyseerd en vervolgens in de **hoofdstukken 2, 3, 4** en **5** beschreven. Gedurende een follow-up periode van 30 dagen na de ingreep werd 36% van alle POWI's na een gastro-intestinale ingreep na ontslag gedetecteerd (**hoofdstuk 2**). Na een vasculaire ingreep bedroeg dit percentage 50% (**hoofdstuk 4**). Uitvoering van surveillance na ontslag heeft dus tot een duidelijke toename van het aantal geregistreerde POWI's geleid. Deze cijfers onderstrepen het belang van surveillance na ontslag.
In de literatuur is er een grote variatie in percentage POWI beschreven, wat o.a. afhankelijk is van de soort chirurgische ingreep, van verschillen in risicofactoren voor POWI's, maar ook van de verschillen in surveillance methodiek. Surveillance kan zowel passief als actief worden uitgevoerd. In ons onderzoek is tijdens opname een actieve surveillance uitgevoerd, na ontslag een passieve surveillance. Tevens zijn infecties onderverdeeld in oppervlakkige, diepe en anatomische infecties en zijn de wonden geclassificeerd in verschillende wondklassen: schoon, schoon-gecontamineerd, gecontamineerd of vies. Deze onderverdeling is van belang vanwege het verschil in ernst van de infectie. Immers, diepe POWI's zijn veel ernstiger dan oppervlakkige, vereisen vaak intraveneuze antibiotica behandeling en leiden tot een langere opnameduur en wondbehandeling. Daarnaast is het risico op een infectie hoger in wonden met een hogere wondklasse (gecontamineerd of vies) vergeleken met schone wonden.

Risicofactoren
Een ander belangrijk aspect van surveillance is de analyse van risicofactoren, afhankelijk van de verschillen in patiënt case-mix. Denk bijvoorbeeld aan verschillen tussen ziekenhuizen en operatieve procedures. Sommige ingrepen zijn complexer of urgenter dan andere. Risicofactoren kunnen dan ook zowel wel of niet vermijdbaar zijn, sommige risico factoren zijn patiënt specifiek, terwijl andere operatie- of omgevings-gerelateerd zijn. In de **hoofdstukken 2, 4** en **5** zijn risicofactoren voor POWI's in de verschillende patiëntenpopulaties beschreven. In **hoofdstuk 2** zijn de risicofactoren voor POWI's in de gastro-intestinale patiëntengroep geanalyseerd; oudere patiënten en patiënten met gecontamineerde of vieze wonden hadden een hoger risico voor het ontwikkelen van een POWI vergeleken bij jongere patiënten met schone wonden. De risicofactoren voor de vasculaire patiëntengroep waren diabetes, leeftijd ouder dan 60 en hogere wondklasse (**hoofdstuk 4**). Hoewel patiënten ouder dan 65 jaar een

hogere kans hadden op sarcopenie, werd geen associatie gevonden tussen sarcopenie en het ontwikkelen van POWI's (**hoofdstuk 5**).
De risicofactoren voor POWI's die tijdens deze studie zijn gevonden zijn deels vergelijkbaar met andere studies. De verschillen in resultaten worden verklaard door o.a. de grote verscheidenheid in operatieve procedures, de case-mix van patiënten met verschillende risicofactoren en het ontbreken van bepaalde patiënten data (ASA klasse, operatieduur) voor een adequate risicoanalyse.

Microbiologie
Tenslotte werd gedurende deze studie aandacht besteed aan de antibiotica gevoeligheid van de uit post-operatieve wonden geïsoleerde micro-organismen. Veel POWI's worden veroorzaakt door micro-organismen die reeds bij de patiënt aanwezig zijn, zoals *Staphylococcus aureus* en *Escherichia coli*. Het ontstaan van een POWI is afhankelijk van verschillende factoren, zoals de locatie van de wond en het aantal en de virulentie van de micro-organismen. In de **hoofdstukken 3, 4** en **5** worden de microbiologische data beschreven in de verschillende onderzochte patiëntenpopulaties. De meest voorkomende micro-organismen in de verschillende patiënten populaties waren *Escherichia coli*, *Pseudomonas aeruginosa* en *Staphylococcus aureus.* Het antibiotica-resistentiepatroon van de micro-organismen werd bepaald door de wondkweken, afgenomen binnen de eerste 48 uur na de operatie, te vergelijken met de wondkweken die daarna zijn afgenomen tot 30 dagen na de operatie. We zagen geen significante toename in antibiotica resistentie binnen deze follow-up periode van 30 dagen werd gevonden. Om het antibiotica-resitentiepatroon in een bepaald ziekenhuis te bepalen, is analyse van een voldoende hoog aantal kweken in het laboratorium, gekoppeld aan het antibiotica gebruik, vereist.
Variatie in microbiologische data in de literatuur kan o.a, (deels) verklaard worden door verschil in antibiotica gebruik van de patient, de virulentie van het micro-organisme, maar ook de afweer van de patiënt zelf speelt een belangrijke rol bij het al dan niet optreden van een infectie.

Conclusie
Dit proefschrift toont aan dat infectieregistratie tijdens en na opname cruciaal is om een betrouwbaar inzicht te verkrijgen in het voorkomen van POWI's na een chirurgische ingreep. Registratie door eenzelfde ervaren, onafhankelijk persoon is

hierbij essentieel. Het onderzoek laat geen verlaging zien in het infectiepercentage na implementatie van de VMS bundel.

Infectiepreventie wordt steeds belangrijker in de dagelijkse praktijk. Er is doorgaans meer vraag en aandacht voor scholing, samenwerking tussen verschillende disciplines (arts-microbiologen, chirurgen, verplegend personeel, ziekenhuishygiënisten) voor het uitvoeren van surveillance studies en, indien nodig, interventies te ontwikkelen. Het is daarom des te belangrijker dat informatie betreffende infectie prevalentie cijfers duidelijk en gemakkelijk toegankelijk zijn om zo adequate interventies op te zetten en de patiënten zorg te verbeteren.

Concluderend, voor een succesvolle implementatie van infectiepreventieve maatregelen is een multidisciplinaire benadering essentieel. Activiteiten gebaseerd op infectiepreventieve protocollen behoren geïntegreerd te zijn in de dagelijkse praktijk en dienen nageleefd te worden door alle zorgmedewerkers. Continue feedback is nodig voor een optimale bewustwording van de consequenties voor de patiënt wanneer richtlijnen niet accuraat worden opgevolgd. Tenslotte, ook hier geldt, voorkomen is beter dan genezen!

List of Abbreviations

ASA	American Society of Anaesthesiologists
BIA	Bio-Impedance Analysis
BMI	Body Mass Index
CAPHRI	School for Public Health and Primary Care
CaRe	Netherlands School of Primary Care Research
CDC	Centers for Disease Control and Prevention
CEA	Carcino Embryonic Antigen
CI	Confidence Intervals
CRP	C-Reactive Protein
CT	Computed Tomography
DXA	Dual energy X-ray Absorptiometry
EUCAST	European Committee on Antimicrobial Susceptibility Testing
ESBL	Extended-Spectrum Beta-Lactamase
FDR	False Discovery Rate
HAI	Health care-associated infection
HB	Haemoglobin
HU	Hounsefield Unit
IBD	Inflammatory Bowel Disease
ICN	Infection control nurse
IRR	The inter-rater reliability
L3	Third Lumbar vertebral level
LOS	Length of Stay
MQ	Muscle Quality
MUMC+.	Maastricht Universiteit Medisch Centrum
MUST	Malnutrition Universal Screening Tool
MRI	Magnetic Resonance Imaging
NFU	Dutch Federation of University Medical Centers (Dutch: Nederlandse Federatie van Universitair Medische Centra
NHSN	The National Health care Safety Network
NNIS	National Nosocomial Infections Surveillance
NVZ	Dutch Society of Hospitals (Dutch: Nederlandse Vereniging van Ziekenhuizen)
OR	Operating Room
OR	Odds Ratio

PAD	Peripheral Artery Disease
PDS	Postdischarge surveillance
PDSA	Plan Do Study Act
PREZIES	Dutch: Preventie van Ziekenhuisinfecties door Surveillance
SENIC	Study on the efficacy of nosocomial infection control
SSI	Surgical Site Infection
SWAB	Dutch working party on Antibiotic policy (Dutch: Stichting Werkgroep AntibioticaBeleid
VMS	Dutch: VeiligheidsManagementSysteem
V&VN	Dutch Association of Medical Specialists and Nurses & Carers (Dutch: Verpleegkundigen & Verzorgenden Nederland)
WHO	World Health Organization
WIP	Dutch Working Party on Infection Prevention (Dutch: Werkgroep InfectiePreventie

Dankwoord

Dankwoord

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Curriculum vitae

Curriculum Vitae

Amita Ramcharan werd geboren op 11 juni 1986 in Noord-Brabant en zij groeide op in Eindhoven. Van 1998 tot 2004 heeft zij het middelbaar onderwijs gevolgd aan het Augustinianum te Eindhoven. In 2004 is ze gaan studeren in Maastricht en startte zij met de opleiding Rechten aan de Universiteit van Maastricht. Toen ze besefte dat dit niet haar passie was, besloot ze Gezondheidswetenschappen te gaan studeren in 2005. Tijdens deze opleiding heeft ze haar kennis en vaardigheden ontwikkeld door als vrijwilliger naar Nicaragua te gaan om daar een onderwijsproject op te zetten voor risico-leerlingen in het dorp Rama, ze heeft in het bestuur gezeten van een studentensportvereniging en ze heeft voor haar Master scriptie onderzoek verricht naar dementia bij ouderen in Seattle, VS.

Na haar opleiding heeft ze kort als onderzoeksassistent gewerkt aan een donorregistratie-project in de afrondende fase. Daarna heeft ze de overstap gemaakt naar ZonMw in Den Haag. Daar heeft ze gedurende een half jaar ervaring opgedaan als staf-assistent Algemeen Beleid. Vervolgens wekte een promotieonderzoek in het Maastricht Universitair Medisch Centrum, op de afdeling van de Medische Microbiologie, haar interesse. Gedurende 4 jaar heeft ze kwantitatief onderzoek verricht naar risico factoren voor en de preventie van post-operatieve wondinfecties, onder leiding van Ellen Stobberingh, Frank van Tiel en em. Prof. Dr. Cathrien Bruggeman. De resultaten van dit onderzoek zijn te lezen in dit proefschrift. Sinds 1 september van dit jaar is ze werkzaam als consultant Financial Services bij Capgemini. Momenteel is ze (nog) woonachtig in Maastricht samen met haar vriend Ivo Smits.

List of publications

Ramcharan A, Penders J, Smeets E *et al.* A cross-sectional study on surveillance of surgical site infections after vascular surgery. *Future Microbiol.* 8(11), 1373–1380 (2013)

Ramcharan A, Smeets E, Rouflart M *et al*. What determines the (in-) efficacy of a surveillance system to reduce surgical site infections after gastrointestinal surgery? *International Journal of Infection Control*. *2014, v10:i.2*

Ramcharan A, den Heijer C, Smeets E *et al*. Microbiology of surgical site infections after gastrointestinal surgery in the south region of The Netherlands. Future Microbiol, 9(3), 291-298 (2014)

Ramcharan A, Ahmad A, Reisinger K *et al*. Does sarcopenia result in a higher risk for developing surgical site infections after colorectal surgery? *Diseases of the Colon & Rectum (Submitted for acceptance)*

Valorisation of the manuscript

Relevance for society and economy

The prevention of health care associated infections (HAIs) has received lots of public attention during the last decade, since the consequences of these infections have a significant impact on health-related quality of life. The main focus of this manuscript is the onset of surgical site infections (SSIs), the most common HAIs in surgical patients. SSIs, either superficial or deep, result in longer hospital stay, longer absence at work, reduced quality of life, greater likelihood of death due to inadequate or delayed treatment, increased burden on family of infected patients, and additional cost for hospitals due to increased overall health care expenditure. The American Centers for Disease Control and Prevention (CDC) estimates that approximately 500.000 SSIs occur annually in the United States. Studies in the Netherlands have shown that the costs per SSI vary between 1000 euros for superficial to more than 20.000 euros for deep SSIs. It is well known that the costs and outcomes related to SSIs vary by location of the surgical incision and type of surgical intervention, but also by type of hospital and country. This manuscript focusses on the prevalence of SSI among gastrointestinal and vascular patient populations in a University hospital in the Netherlands.

The risk for infections and the spread in- and outside the health care facility depend in part on the (adequate) attention for infection preventive policy in hospitals. The lessons learned underscore the importance to educate health care professionals about the increasing problem of antibiotic resistance and the relevance to control the increasing rate of resistance. It is important for health care institutions to continue to improve their policy regarding infection prevention and antibiotic use to minimise the risk on HAI as much as possible. The main reasons for this are the increased costs, morbidity, and mortality in patients with infections due to resistant versus susceptible organisms, which are higher in the first group.

The goals of this study were to 1) get insight into the infection prevention policy, 2) to determine the prevalence in SSI rates in different patient populations, 3) to determine the quality of care for surgical patients with regards to infection preventive measures, 4) to analyse risk factors to develop SSIs, 5) to investigate antibiotic patterns of the causative microorganisms of SSI in surgical patients, and

6) to formulate infection preventive measures, based on the study results, for health care providers, future infection preventive researchers, and other involved parties.

Target groups

Nowadays, policy regarding infection prevention in health care facilities is becoming increasingly important for different target groups, i.e., for all involved health care professionals and for the patients and their family. It is therefore important for scientific researchers to perform studies on the topic. Adequate communication between different disciplines (infection prevention experts, surgeons and anesthesiologists, microbiologists, nursing staff) is an important tool to implement infection prevention policy. Hereby, infection control professionals carry the main task to stimulate communication about practical implications of infection control in a health care setting. And as antibiotic resistance is a major concern to the society as a whole, it is important to educate or train the professional, the patient and the society about infection control and proper antibiotic use, starting at the primary school.

Activities

There are many activities to think of in order to stimulate infection prevention. For instance, the implementation of infection preventive programs according to the Plan-Do-Study-Act (PDSA) cycle, the implementation of a care bundle (e.g., VMS bundle), infection registration during hospitalisation and after discharge, audit and feedback, and education on infection control and on antibiotic resistance.
Many studies have shown that hospital infections are preventable with simple measures, such as better hand hygiene and correct administration of antibiotic prophylaxis. Moreover, the on-going and long-term promotion of infection prevention measures is essential for a successful implementation and to measure the compliance with infection preventive policies. The implementation of infection preventive measures should therefore become a standard of quality patient care within health care institutions. Senior staff members (e.g., medical consultants, nurse managers, managers in the health professional groups, and other role models) should actively promote infection prevention policy.

Another current phenomenon investigated for this manuscript, is that the postoperative hospital stay is shortened, and that more outpatient surgeries and same-day surgeries are carried out. This results in more SSIs diagnosed after discharge from the hospital. Consequently, more SSIs are missed with infection control surveillance programs when performed only during hospitalisation. Thus, for reliable data concerning the prevalence of HAI in general, SSI in particular, surveillance activities need to be performed during and after hospitalisation.

Regarding infection preventive measures, monitoring the compliance with these measures should be continuously carried out in order to control the risk and safety framework of health care institutions. And again, this can be performed through audits with feedback of results.

The patient's health care environment can also be a source of contamination. Each contact with hospital furniture, doors, and many medical devices can be a major risk to patients. Sterilisation is needed for surgical instruments and other devices, but it is not necessary for all items and surfaces.

As infection prevention policy is an essential component of care, all health care workers who work in the surgical environment must be educated in infection preventive theory and techniques prior to their work related actions. This can be achieved through an infection control component within the introduction program for which attendance must be mandatory. Furthermore, undergraduate medical, nursing, infection prevention practice, and other surgical health care course curricula should include education and examination theory and techniques. There are a variety of options to educate when it comes to reliable resources, for instance: local and online information, study days, conferences, courses, practice and e-learning resources, the health care industry or commercial companies, and professional organisations (e.g., the Centers for Disease Control and prevention (CDC), the Dutch PREZIES network, the Infection Prevention Society (IPS), and the Healthcare Infection Society (HIS)).

With regards to the antibiotic resistance, it is important to analyse the antibiotic resistance patterns and to know common errors physicians are dealing with when prescribing antibiotics. For the physicians, by prescribing antibiotics without properly diagnosing an illness or without properly weighting the consequences of the antibiotics, they are promoting antibiotic resistance in their patients and society as well.

Efforts to describe the global impact of antimicrobial resistance are hampered by the lack of data on the impact of resistance outside the hospital settings. There has

been little, if any, effort to assess the larger societal and macroeconomic costs of resistance, especially in the developing world, related to lost wages, the costs of caring for patients with SSI, and the impact of increased mortality, or the costs for surveillance and other infection preventive interventions. Treatment failure is another contributor to increased health care costs and can lead to additional investigations, additional or alternative treatments, often much more expensive than drugs used to treat infections caused by sensitive organisms. Thus, more research should be performed to deal with these issues.

Innovation based on existing knowledge and offer

Risk factors for SSI can be differentiated into those which are modifiable and those which are not. During the study period of this manuscript, the Dutch VMS safety care bundle was implemented. The general goals of care bundles are to enable staff to quickly see what actions should be taken, when and by whom. Furthermore, care bundles allow clinical practice to be standardised and reduce variation in the treatment plans for patients.

The VMS bundle consisted of a small set of evidence-based interventions for surgical patients and care setting that, when implemented together, aimed to result in significantly better outcomes than when implemented individually. The bundle allowed us to focus our efforts on four measurable strategies: no skin shaving before surgery, administration of antibiotic prophylaxis (adequate choice, dose and timing), normothermia, and restriction of entry in the operating theatre. The number of door movements of the operating theatre contributes to an increased number of microorganisms in the air and to an increased risk on an infection.

Implementing a bundle of care with high reliability requires redesign of work processes, communication strategies, and infrastructure, along with compliance measurement. This requires high quality of care to ensure that the surgeons' judgement is supported by best available practice evidence at the point of care, and that barriers of implementation of evidence based results are reduced.

Finally, postdischarge surveillance, as mentioned above, results in more identified SSIs among surgical patients. It has been demonstrated that hospitals with comprehensive postdischarge surveillance after surgical procedures are likely to record higher SSI rates than those that do not perform such surveillance.

Planning and realisation

As previously mentioned, many activities can be carried out to prevent infections (e.g., implementation of infection preventive programs according to the PDSA cycle, implementation of a care bundle, infection registration during hospitalisation and after discharge, audit and feedback, and education on infection control and antibiotic resistance). However, the timeframe is situation-dependent.

Recommendations towards infection prevention are known; routine observation and feedback, education to health care staff and patients, reminders at the workplace, administrative sanctions, and rewards. Furthermore, it is important to obtain active participation at individual and institutional level in order to ensure a safety climate, to enhance self-efficacy, and to avoid understaffing and workload.

With regards to the use of antibiotics, measuring the impact of drug resistance is an important step in understanding the scope of the problem, and to develop policies to limit the emergence and spread of resistant microorganisms. Although there is little doubt that antimicrobial resistance is increasing the global burden of disease, we are a long way from being able to quantify this burden.

To conclude, this manuscript adds more insight into infection prevention policy for surgical patients and health care workers. Since SSIs are unintended and in some cases preventable, it is recommended to establish multidisciplinary teams and to provide feedback to the involved parties. It is up to practitioners in each health care setting to review the evidence and work together to implement SSI preventive interventions. There are two main activities related to infection prevention. The first is to encourage infection prevention, for which the measures are to develop infection preventive guidelines for health care facilities, and to implement these guidelines. In this regard, the target group is the personnel of the facility. The second main activity is the surveillance of SSIs by systematically gather, analyse, and report infection rates. In this regard, the target groups are all health care personnel and the (surgical) patients. The executors involve the WIP, SWAB, microbiologists, and infection control professionals.

The benefits of preventing SSIs are the decreasing patient mortality and the decreasing burden that SSIs pose on the national health care system. Therefore, it is up to all health care workers to continue supporting SSI prevention initiatives!

“Live as if you were to die tomorrow. Learn as if you were to live forever”

Mahatma Gandhi

This manuscript describes elements for an accurate infection registration method. Surgical site infections (SSIs) acquired after surgery may be serious and, in some cases, life-threatening. These may result in higher morbidity and adversely affect recovery.

SSIs may be caused by organisms that are resistant to antibiotics. It is therefore important that clear information on the standards of infection prevention and control in hospitals is combined and easily available to allow adequate surveillance and to improve the quality of care.
For the prevention and control of SSIs, and a successful implementation of a safety bundle, a multidisciplinary approach is crucial. Activities based on infection prevention protocols should be imbedded in every day practices and adhered to by all health care workers. Through feedback they have to be made aware of the consequences for the patient when guidelines are not recognised and followed accurately. Besides the availability of tools, education, communication and support, leadership and active involvement are important aspects.

The first steps in SSI prevention are the willingness, collaboration, and efforts to improve compliance with infection preventive measures.

After all: an ounce of prevention is worth a pound of care!

Amita A. Ramcharan